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# ICRDB CANCERGRAM

# RADIATION CARCINOGENESIS

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## RADIATION CARCINOGENESIS IN HUMANS

### 1. BRONCHO-ALVEOLAR LAVAGE IN URANIUM MINERS.

**Robalo Cordeiro AJ, Bahanha MF, Carmo JG, Gaspar E, Lima MA, Rosa MA**
**Universite de Coimbra, 3049 Coimbra, Portugal**
**Rev Fr Mal Respir; 9(3):241-256 1981**

The effects of tobacco smoking plus occupational exposure to uranium were studied in 32 uranium miners (M: 16 smokers (S), and 16 nonsmokers (NS)) and 12 controls (C: 6 S and 6 NS) through the use of broncho-alveolar lavage (BAL). The percentages of liquid in the fluid obtained by BAL was signifi-

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cantly different in the two groups of M. Differences in the number of macrophages (MA) were observed in M and C. The MA of S showed characteristics similar to other smoking populations in this group of M. In general the size of the MA of S were larger than those of NS. The viability of MA in the various groups was studied. No statistically significant differences were observed between the groups analyzed for phagocytosis by MA. The results did not permit the determination of differences between MA of M and C with regard to adherence to glass. The migration of MA was variable in the groups studied. No significant differences were observed between S and NS with regard to peripheral blood lymphocytes. The phytohemagglutinin stimulation of lymphocytes was generally more elevated in those of the blood as compared with those of the BAL fluid, with significant differences in the NS. The IgG of the BAL fluid of M was more elevated in S and was significantly different from control levels. IgA levels were decreased in the smoking group of M. No variation in BAL fluid albumin or total proteins was observed for the four groups. The results indicated that there were no demonstrable changes in cellular function in either S of NS in M subjected to the ambient radiation of a uranium mine. (37 Refs) (In FRE)

## 2. SKIN CANCER IN PATIENTS WITH PSORIASIS TREATED WITH COAL TAR.

**Pittelkow MR, Perry HO, Muller SA, Maughan WZ, O'Brien PC**
**Section Publications, Mayo Clinic, 200 First St. SW, Rochester, MN, 55905**
**Arch Dermatol; 117(8):465-468 1981**

For many yr, crude coal tar has been used for the treatment of psoriasis. The possible carcinogenic effect of crude coal tar and UV radiation (Goeckerman regimen), considered individually or in combination, has been of some concern to physicians. A 25 yr follow-up study was completed on 280 patients with psoriasis who were hospitalized and treated with crude coal tar and UV radiation at the Mayo Clinic, Rochester, Minnesota during the yr 1950 through 1954. The results of this study suggest that the incidence of skin cancer is not appreciably increased above the expected incidence for the general population when patients are treated with coal tar ointments. It seems that the Goeckerman regimen (topical crude coal tar combined with UV radiation) can be used with minimal risk for skin cancer in the treatment of psoriasis. (Author abstract) (22 Refs)

## 3. PUVA (PSORALEN AND ULTRAVIOLET A) AND SQUAMOUS CELL CARCINOMA IN PATIENTS WITH PSORIASIS (MEETING ABSTRACT).

**Stern RS, Parrish JA, Bleich HL, Fitzpatrick TB**
**Harvard Medical School, Boston, MA**
**J Invest Dermatol; 76(4):311 1981**

In the initial 2 yr, 30 patients with psoriasis exposed to PUVA developed cutaneous carcinoma. Now, after 4 yr of prospective study 73 of 1140 (6.5%) patients over age 30 have developed a total of 145 cutaneous carcinomas. Of these 73, 40 patients had a total of 96 squamous cell carcinomas (SCC). While the incidence of basal cell carcinoma (BCC) was only modestly elevated, the observed incidence of SCC was 9.1 x that expected based on age, sex, and geographically specific rates. While there was no apparent relation of the number of PUVA treatments and the risk of BCC, after 80 PUVA treatments the relative rate developing a SCC compared to a BCC was 5-fold greater. No dose dependent increase in the relative risk of SCC was noted in those patients who were not previously exposed to cutaneous carcinogens. Comparing SCC and BCC patients, patients with SCC were younger, had more PUVA treatments prior to first tumor, had prior exposure to ionizing radiation (53% vs 44%), or prolonged exposure to tar and UVB light (69% vs 44%), and had more tumors. These data suggest that PUVA acts as a promotor of SCC in humans previously exposed to cutaneous carcinogens; an effect that increases with higher numbers of PUVA treatments. (no Refs)

## 4. EPIDEMIOLOGIC STUDY OF ETIOLOGIC FACTORS IN PROSTATIC CANCER (VOLUMES I AND II).

**Mandel JS**
**University of Minnesota, Minneapolis, MN**
**Diss Abstr Int (B); 42(1):155-B 1981**

This was a case-control study exploring a number of factors of possible significance in the etiology of prostatic cancer. Cases were white men under the age of 75 with a newly diagnosed prostatic cancer. A sample of blood and a first morning urine specimen were obtained from every study subject. An extensive personal interview was conducted on the following factors: residence, smoking, alcohol consumption, use of medications, prior medical history, radiation exposure, previous hospitalizations, family history of cancer, marital history, and patterns of sexual behavior. In addition, each subject completed a self-administered frequency of use dietary questionnaire. The bloods were analyzed for antibodies to herpes, cytomegalic and Epstein-Barr virus. In addition, endocrine assays were done for prolactin, luteinizing, follicle-stimulating, and thyroid stimulating hormones. Prostatic cancer cases were slightly more educated and smoked fewer cigarettes than controls. With respect to patterns of sexual behavior, cases had generally experienced less sexual activity than controls. A number of medical conditions and surgical procedures were associated with prostatic cancer. Asthma, kidney stones, urinary infections, veneral disease and mumps were positively associated with prostatic cancer. Liver disorders, heat trouble and stroke, although not statistically significant, were less often reported by cases than controls. A greater proportion of cases than controls had had a tonsillectomy or adbominal surgery. On the other hand, appendectomy, gallbladder surgery and hernia repair were less frequent among the cases. The consumption of liver, coffee, and carrots was more common among the controls than among the cases. Bread, potatoes and packaged cereals were consumed more often by cases than controls. A significant circannual rhythm for thyroid stimulating hormone found for men at low risk of developing prostatic cancer was not found for men at high risk of developing prostatic cancer or for men with prostatic cancer. For prolactin, a significant circannual rhythm was found for cases but not for controls. (no Refs)

## 5. RADIATION EFFECTS ON THE ADULT THYROID GLAND (MEETING ABSTRACT).

**Kinsella TJ, Glatstein E**
**Radiation Oncology Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD**
**Long Term Normal Tissue Effects of Cancer Treatment, April 13-15, 1981, Bethesda, Maryland Committe for Radiation Oncology Studies; 1981**

The development of thyroid disease, including thyroid nodules and thyroid carcinoma, following radiation exposure is well known. However, most the clinical data are derived from patients irradiated for benign conditions with low doses of radiation in infancy or early childhood. From these data, there appears to be an inverse relationship of radiation carcinogenesis to age and the total dose of radiation. Conversely, in older patients receiving high dose irradiation in the treatment of nonthyroidal malignancy, thyroid hypofunction appears to be the major radiation complication. We have recently evaluated 5 patients with Hodgkin's Disease treated with mantle irradiation in the 2nd decade of life who presented with thyroid nodules from 8 to 22 yr following irradiation. Three cases of thyroid carcinoma were found. These cases will be used to highlight the histologic spectrum of radiation injury to the adult thyroid as well as the controversies in the diagnostic and therapeutic management of these patients. (no Refs)

## EXPERIMENTAL RADIATION CARCINOGENESIS

### 6. NEOPLASIA IN FAST NEUTRON-IRRADIATED BEAGLES.

**Bradley EW, Zook BC, Casarett GW, Deye JA, Adoff LM, Rogers CC**

**Dept. Radiology, George Washington Univ. Medical Center, Washington, DC, 20037**

**JNCI; 67(3):729-738 1981**

One hundred fifty-one beagle dogs were irradiated with either photons or fast neutrons (15 MeV) to one of three dose-limiting normal tissues - spinal cord, lung, or brain. The radiation was given in four fractions per wk for 5 wk (spinal cord), 6 wk (lung), or 7 wk (brain) to total doses encompassing those given clinically for cancer management. To date, no nonirradiated dogs or photon-irradiated dogs have developed any neoplasms. Seven dogs receiving fast neutrons have developed nine neoplasms within the irradiated field. Of the neutron-irradiated dogs at risk, the incidence of neoplasia was 15%. The latent period for radiation-induced cancers has varied from 1 to 4 1/2 yr at this time in the study. (Author abstract) (33 Refs)

### 7. ULTRAVIOLET RADIATION-INDUCED NEOPLASTIC TRANSFORMATION OF NORMAL HUMAN CELLS, IN VITRO.

**Milo GE, Weisbrode SA, Zimmerman R, McCloskey JA**

**Dept. Physiological Chemistry, Comprehensive Cancer Center, Ohio State Univ., 19 00 Coffey Road, Columbus, OH, 43210**

**Chem Biol Interact; 36(1):45-59 1981**

Human foreskin cell cultures in scheduled DNA synthesis (S phase) of the cell cycle were exposed to UV irradiation at a dose of 10 J x m-2 in the presence of insulin. These treated cell populations, when selectively passaged in a high amino acid supplemented complete growth medium (CM) after 20 Dulbecco's phosphate buffered saline (pH 6.8) (PDL), were able to be grown in soft agar. These treated cell populations were also grown in 1% serum supplemented growth medium and at 41 C in 10% serum supplemented growth medium. Cell populations 4-5 PDL after treatment exhibited altered colony morphology and altered lectin agglutination profiles but would not grow in soft agar. These events appeared to be associated with the early stages in the expression phase of the transformed phenotype. After 20 PDL, we observed that these cells would grow in soft agar at a frequency of 20 colonies/10(5) cells seeded in soft agar. The cell populations derived from these colonies, when propagated and injected into the nude mice, formed myxofibromas at the injection sites rather than the type of tumor (fibrosarcoma) previously described for chemical carcinogen-induced neoplasms. (Author abstract) (18 Refs)

### 8. LACK OF ENHANCEMENT OF EXPERIMENTAL PHOTOCARCINOGENESIS BY TOPICAL RETINOIC ACID.

**Kligman LH, Kligman AM**

**Duhring Lab., Dept. Dermatology, Univ. Pennsylvania Sch. Medicine, 36th and Hamilton Walk, Philadelphia, PA**

**Arch Dermatol Res; 270(4):453-462 1981**

The ability of retinoic acid (RA) to enhance UV carcinogenesis was studied in lightly pigmented hairless mice. In the first series of the experiments, animals were subjected to 30-wk UV irradiation and concomitant topical administration of RA followed by 15-wk RA administration. In the second series of the experiments, animals received UV irradiations alone for the first 30 wk and then RA alone for the next 15 wk. UV irradiation induced multiple skin papillomas in 100% of the animals. RA administration (either concomitantly with UV or after tumor induction) did not affect the latent period, tumor yield or tumor progression. (39 Refs)

### 9. ENDOCRINE OPEN DISCUSSION: QUANTITATIVE ASSESSMENT OF THYROID CELL SURVIVAL AND CARCINOGENESIS USING AN IN VIVO TRANSPLANTATION ASSAY (MEETING ABSTRACT).

**Mulcahy RT, Clifton KH**

**University of Rochester Cancer Center, Rochester, NY**

**Long Term Normal Tissue Effects of Cancer Treatment, April 13-15, 1981, Bethesda, Maryland Committe for Radiation Oncology Studies; 1981**

The survival of rat thyroid epithelial cells irradiated in vitro or in vivo was assayed with our recently developed in vivo transplantation assay. Survival was the same for cells irradiated in vitro after enzymatic dispersion and for cells irradiated in situ and dispersed five min after irradia tion. Under these conditions the dose was determined to be 198 rad, and n and 4. The dose for thyroid cells irradiated and left in situ was 197 rad. However, the survival curve has a much larger shoulder with correspondingly increased n and D q values. These findings indicate that the survival of irradiated thyroid cells is enhanced when the tissue is allowed to remain in its normal arrangement for 24 hr after irradiation. These findings further demonstrate that thyroid epithelial cells are more sensitive to radiation than has been previously thought. This may be related to the recently recognized thyroid abnormalities produced following certain therapeutic radiation treatments. Using the same transplantation technique we have assessed the relative risk of thyroid tumor induction following radiation exposure. Following exposure to 500rad X-radiation, there was approx a 3.5 fold increase in carcinoma induction in thyroidectomized rats injected with irradiated thyroid cells relative to rats injected with unirradiated cells. This technique has great potential for quantitative studies related to cancer therapy, thyroid carcinogenesis and to the biology of cell renewal and differentiation. (no Refs)

### 10. SURVIVAL OF MAMMARY EPITHELIAL CELLS FROM VIRGIN FEMALE BALB/C MICE FOLLOWING WHOLE BODY GAMMA IRRADIATION (MEETING ABSTRACT).

**Adams LM, Ullrich RL**

**Biology Division, Oak Ridge National Lab., Oak Ridge, TN, 37830**

**4th Annual San Antonio Breast Cancer Symposium, Nov 6-7, 1981, San Antonio, Texas Cancer Therapy and Research Center of South Texas; 1981**

The tumorigenic dose response to radiation in mammary epithelium is confounded by cytotoxic effects on target mammary cells and by effects on other systems which influence expression of transformed mammary cells. A method to examine both cytotoxic and initiating effects on target cells alone is now being used in our laboratory. Mammary cells are enzymatically dissociated from the fat pads of mice exposed twenty-four hr previously to 0, 100, 300, 600 or 900 rads whole body 137Cs gamma radiation. Cells are serially diluted and 10 2 to 10 3 cells are injected into gland-free fat pads of 3-wk-old syngeneic BALB/C female mice. Fat pads are scored for growth at three wk. In this manner a classic cell survival curve is generated. Since outgrowths fill only about ten percent of the fat pad by three wk, these studies are now being extended using a ten-wk endpoint so that lesions as well as growth can be scored. By combining the cell survival data and the lesion frequency, a transformation frequency based upon the number of viable cells injected can be calculated. (no Refs)

### 11. INDUCTION OF MAMMARY DUCTAL DYSPLASIA BY GAMMA-RAY IRRADIATION OF MAMMARY TISSUES OF VIRGIN FEMALE BALB/C MICE (MEETING ABSTRACT).

**Ethier SP, Ullrich RL**

**Biology Division, Oak Ridge National Lab., Oak Ridge, TN, 37830**

**4th Annual San Antonio Breast Cancer Symposium, Nov 6-7, 1981, San Antonio, Texas Cancer Therapy and Research Center of South Texas; 1981**

The carcinogenic effect of ionizing radiation on mammary epithelium has been difficult to study because the endocrine imbalance which results from whole body exposure modifies the tumor response. This difficulty can be avoided by transplanting mammary cells from an animal that was exposed to radiation to an untreated animal in order to study the growth potential of the cells. We are using this principle to detect abnormal growth potential of mammary cells which were exposed to ionizing radiation. In these experiments 12-wk old virgin female BALB/c mice were exposed to 100 rad of Cs-137 gamma-ray irradiation or were sham irradiated. Twenty-four hr later the mice were killed and the mammary tissues removed. Cells were dissociated by enzymatic procedures and either 10(4) or 10(5) cells were injected into the gland-free mammary fat pads of 3-wk-old virgin female BALB/c mice. This procedure results in ductal mammary outgrowths which fill the fat pad by 10 wk after the injection of cells. Of the outgrowths derived from control cells, 2-3 percent had ductal abnormalities while 15 percent of the outgrowths derived from treated cells were abnormal. These lesions were observed at the whole mount and histological level and were classified as ductal dysplasia. This procedure allows the detection and study of altered growth potential of mammary epithelial cells induced by the direct action of ionizing radiation. Further, the mammary lesions which were observed in this study resemble preneoplastic mammary lesions which have been observed in chemical carcinogen treated rats and mice. (no Refs)

### 12. THE PRESENCE OF 8.0 AND 5.6 KB GENOMIC RNA IN MULV ISOLATED FROM PRIMARY X-RAY IRRADIATION INDUCED THYMOMAS (MEETING ABSTRACT).

**Sankar-Mistry P, Lemay G, Jolicoeur P**

**Institut de rechercehes cliniques de Montreal, Montreal, Quebec, Canada**

**RNA Tumor Viruses, May 20-24, 1981, Cold Spring Harbor, New York Cold Spring Harbor Laboratory 294 pp., 1981.**

We have reported the isolation of a murine leukemia virus (MuLV) from continuous lymphoid cell lines established from primary X-irradiation induced C57BL/Ka thymoma. One of the isolates (G6T2) which is produced by these lymphoid cells, has been characterized further. It is XC+ and is able to replicate on fibroblasts and thymocytes in vitro. It is leukemogenic when reinjected into newborn C57BL/Ka mice and induces T-cell lymphomas within 10-12 mo. G6T2 replicates well in SC-1 cells: the fibrotropic progeny virus (SC-1/G6T2) is also leukemogenic when reinjected into newborn C57BL/Ka mice and induces T-cell lymphomas within 7-10 mo. A cell line, established from one of these SC-1/G6T2 induced lymphomas, produces large quantities of MuLV that retain the B-tropism and XC+ phenotype. We have analyzed the genomic RNA of G6T2 using the agarose gel/transfer procedure and found two viral RNAs of 8.0 and 5.6 kilobase (kb). By the same technique, we have also looked for viral RNA in primary X-irradiation induced thymomas and found a prominent 5.6 kb viral RNA species. Our results show that X-irradiation induced lymphoma cells express leukemogenic fibrotropic (and thymotropic) MuLV containing two RNA genomes. By analogy with other avian retroviruses and the Abelson MuLV, we suggest that the shorter RNA genome might harbor a gene responsible for T-cell transformation and for the development of lymphoma in irradiated C57BL/Ka mice. (1 Ref)

### 13. XENOTROPIC MULV EXPRESSION IN THYMOMA AS INDUCED BY RADIATION OR METHYLCHOLANTHRENE (MEETING ABSTRACT).

**Mayer A**

**Department of Pathology, New York University Medical Center, New York, NY**

**RNA Tumor Viruses, May 20-24, 1981, Cold Spring Harbor, New York. Cold Spring Harbor Laboratory 294 pp., 1981.**

Thymic lymphoma incidence and thymic xenotropic MuLV expression was monitored in AKR, RF, and reciprocal Fl mice of the AKR x RF cross after treatment with either gamma-radiation or the chemical carcinogen 3-methylcholanthrene (MCA). These two inbred strains and their Fl hybrids developed similarly high incidences of thymoma, and lymphomatous cells from AKR mice and (AKR x RF) Fl mice were observed to be expressing MuLV with xenotropic host range. However, lymphoma cells from RF mice did not produce detectable levels of xenotropic MuLV. Thymic xenotropic virus expression was therefore not correlated with a high incidence of radiation- or chemically-induced thymoma, but rather appeared to be genetically transmitted by AKR mice to Fl mice of the AKR x RF cross as a dominant trait in induced thymomas. In addition, a maternal effect on thymic xenotropic virus expression in induced thymomas was observed by the comparison of reciprocal Fl hybrids in this cross. (no Refs)

## EXPERIMENTAL RADIATION MUTAGENESIS

### 14. THE EFFECT OF A CHANGE IN MUTATION RATE ON THE INCIDENCE OF DOMINANT AND X-LINKED RECESSIVE DISORDERS IN MAN.

**Childs JD**

**Health Sciences Div., Atomic Energy Canada Ltd., Chalk River Nuclear Laboratories, Chalk River, Ontario KOJ 1J0, Canada**

**Mutat Res; 83(1):145-158 1981**

An estimate of mutation frequency for each of the important dominant and X-linked recessive diseases has been reported in order to obtain a direct estimate of the expected increase in dominant disease for any postulated increase in av mutation frequency. From estimates of birth frequency, spontaneous mutation rate and reproductive fitness, the rate of increase of birth frequency could be calculated for each disease based on any given sustained increase in mutation rate. These disorders affect approx 0.6 % of live-born persons, including 0.1% who carry a newly-arising mutation. The preceding estimated figures are approx 50% lower than those used by various committees that have assessed the genetic risk to man from ionizing radiation. If the mutation frequency were to double, the frequency of these disorders would be expected to increase in the first generation by 15%, to 0.7% of live births; in the first two generations, the increase would be 24%, and in the ninth generation, 50%. Calculation of the possible increase in these disorders due to exposure to ionizing radiation demonstrated that the estimates made in 1977 by the United Nations Scientific Committee on the Effects of Atomic Radiation may be overestimates by a factor of at least 6. (62 Refs)

### 15. A MOUSE-CELL MUTANT SENSITIVE TO IONIZING RADIATION IS HYPERMUTABLE BY LOW DOSES OF GAMMA-RADIATION.

**Shiomi T, Hieda-Shiomi N, Sato K, Tsuji H, Takahashi EI, Tobari I**

**Div. Genetics, Natl. Inst. Radiological Sciences, 9-1, Anagawa-4-chome, Chiba-shi 260, Japan**

**Mutat Res; 83(1):107-116 1981**

Mutation induction after gamma-irradiation was compared in the mutant mouse lymphoma cell M10, which is sensitive to x-rays and methyl methanesulfonate (MMS), and the parental line L5178Y. The M10 cells were more sensitive to the killing effects of gamma-irradiation than the L5178Y cells, and the mutation frequency induced by unit dose of gamma-rays was higher in the mutant cells than in L5178Y cells at doses ranging from 25-145 R. In M10 cells, mutation frequencies per unit dose declined sharply while these values increased in the parental cells at doses ranging from 25-500 R. The selective removal of highly damaged and highly mutable cells from the irradiated cell population caused a progressive decrease in mutation frequency in the mutant cells. In M10 cells, yields of mutation frequency fluctuated considerably over the dose range studied, while no fluctuation was observed in the parental line. It is suggested that the repair process in M10 cells is more mutagenic than that in the parental cells after gamma-irradiation. (13 Refs)

### 16. COMPARISON OF PHOTOMUTAGENIC ACTIVITIES OF 5-MOP (BERGAPTEN) AND 8-MOP (XANTHOTOXIN) IN CHLAMYDOMONAS REINHARDII.

**Schimmer O**

**Institut fur Botanik und Pharmazeutische Biologie, Universitat Erlangen-Nurnberg, Schlossgarten 4, D-8520 Erlangen, W. Germany**

**Mutat Res; 89(4):283-296 1981**

The compounds 5-methoxypsoralen (5-MOP) and 8-methoxypsoralen (8-MOP) which are used for photochemotherapy of psoriasis were investigated in terms of their mutagenicity. The photomutagenic and phototoxic activities were compared in arg negative (arg-) cells of Chlamydomonas reinhardii and their ability to revert to Arg+ mutants. 5-MOP was shown to be more phototoxic than 8-MOP if UV-A irradiation (2 W/square meter (m2) and 2.7 W/m2) was administered to the strains and if the concentration of the compound as well as the original cell number were equal. On the other hand, mutagenicity of both substances increased linearly according to the increase in their concentration if UV-A irradiation was constant. The mutagenic effect of both substances was also dependent on the duration of UV-A irradiation. In both UV-A and white light 5-MOP, however, was effective more rapidly than 8-MOP. Since the minimal effective dose of 5-MOP was reported to be 0.1 ug/ml plus 0.12 Joule/m2, sensitivity of the test object could be compared to that of human lymphocytes in vitro. The minimal effective dose of 8-MOP in human lymphocytes was reported to be 1 ug/ml plus 0.5 Joule/m2. (24 Refs) (In GER)

## EFFECTS OF IRRADIATION ON CHROMOSOMES AND DNA

### 17. CYTOLOGICAL EVIDENCE FOR DNA CHAIN ELONGATION AFTER UV IRRADIATION IN THE S PHASE.

**Minka DF, Nath J**

**Dept. Medical Genetics, Sch. Medicine, Indiana Univ., Indianapolis, IN**

**Biochem Genet; 19(3/4):199-210 1981**

Human xeroderma pigmentosum cells of the XP12BE (XP classic) excision deficient and XP4BE (XP variant) excision proficient cell lines were studied. Cells were synchronized and 1 mM caffeine added. Six sets of plates were irradiated with UV at 0, 1, 2, 3, 4, and 5 hr during S phase. Six hr after the start of S phase, caffeine was removed from the medium. One plate from each set was labeled with 3H-thymidine (3H-TdR) at 0, 0.5, and 1.5 hr after caffeine removal. Controls consisted of untreated cultures and cultures treated with caffeine or UV. XP classic cells with caffeine had greater 3H-TdR incorporation than cells without caffeine when irradiated at the beginning of S phase. Incorporation of the label declined to non-caffeine levels at the end of S phase. Caffeine did not affect labeling in XP variant cells. Human cells irradiated with UV synthesize lower mol wt DNA than unirradiated cells, due to gaps in the DNA. Repair mechanisms eliminate these gaps within a few hr after irradiation. Results of this experiment indicate occurrence of unscheduled DNA synthesis, possibly chain elongation, during the G2 phase in excision deficient cultures. (30 Refs)

### 18. OBSERVATIONS ON THE EFFECT OF X-RAY ALONE AND IN COMBINATION WITH ULTRASOUND ON HUMAN CHROMOSOMES.

**Kunze-Muhl E**

**Institut fur Allgemeine Biologie der Medizinischen Fakultat, Universitat Wein, Schwarzpanierstrasse 17, A-1090 Wien, Austria**

**Hum Genet; 57(3):257-260 1981**

The synergistic effect between ultrasound (US) and ionizing radiation was studied in human peripheral blood lymphocytes. Blood samples were treated with US before or after exposure to x rays (50, 100 or 200 R). The samples were cultured, and the frequency of chromosome aberrations was determined. The yield of chromosome aberrations was found to depend upon the dose, duration, and order of treatment: 10-min exposure to high intensity US before x rays increased the incidence of all types of aberrations, while 10-min exposure to high intensity US after x- rays decreased the yield of minutes and fragments. One-hr exposure to low intensity US after irradiation with 200 R decreased the frequency of chromosome aberrations, compared with significant increase of the frequency of chromosome aberrations recorded in case of 1-hr exposure to low intensity US before irradiation with 200 R. (28 Refs)

## OTHER CELLULAR EFFECTS OF IRRADIATION

### 19. THE EFFECTS OF ULTRAVIOLET IRRADIATION ON THE GENERATION OF ANTI-TUMOR CYTOTOXIC EFFECTOR CELL RESPONSES IN VITRO.

**Lynch DH, Gurish MF, Daynes RA**

**Dept. Pathology, Univ. Utah Medical Center, Salt Lake City, UT, 84132**

**J Immunol; 127(3):1163-1168 1981**

The effects of irradiation of lymphoid cells in vitro with UV light were studied using radiation sources that are widely used both in the study of photocarcinogenic mechanisms and by commercial tanning parlors (FS40 sunlamps). Low doses of direct exposure of cells was found to abrogate the differentiation events that lead to the generation of functional cytotoxic T lymphocytes (CTL). UV irradiation of cells in vitro induces alterations that, although not immediately obvious, lead to cell death during the next several days in tissue culture. Energy titration experiments demonstrated that both primed T cells and accessory cells were sensitive to the effects of direct UV-exposure; T cells were found to be much more sensitive than accessory cells. A 90% decrease in CTL generation could be affected with as little as 10 sec of UV exposure. These effects appear to be caused by wavelengths in the UVB range (280 to 320 nm), since exposure of cells to much higher doses of energy in the UVA range (320 to 400 nm) were not inhibitory. The spectrum of wavelengths in the UV region is large (200 to 400 nm). The data presented here demonstrate that it is overly simplistic to assume that all wavelengths in the UV spectrum mediate their effects via identical mechanisms. Furthermore, the wavelengths at which a given amount of energy is emitted appears to be much more important than the absolute amount of energy (in joules) to which biological systems are subjected. (Author abstract) (22 Refs)

## ENVIRONMENTAL RADIATION AND PROTECTION STANDARDS

### 20. BIOLOGICAL EFFECTS OBSERVED IN MAMMALS MAINTAINED IN AN AREA OF VERY HIGH NATURAL RADIOACTIVITY.

**Leonard A, Delpoux M, Chameaud J, Decat G, Leonard ED**
**Lab. Mammalian Genetics, Dept. Radiobiology, C.E.N.-S.C.K., B-2400 Mol, Belgium**
**Can J Genet Cytol; 23(2):321-326 1981**

Male rabbits (Oryctolagus cuniculus) were maintained for a 28-mo period on the floor of a hut built at a site in southwestern France where the dose rate from natural radioactivity amounts to about 8 mrad/h. Male and female BALB/c mice (Mus musculus) were also placed in the hut during the summer period. The observations performed on those animals demonstrate that exposure to high natural radiation can increase the frequency of chromosome aberrations in somatic cells and indicate also that fertility in males and females is affected in an inverse manner. Model experiments with radon exposure of laboratory rabbits under controlled conditions have shown that the chromosome aberrations observed in somatic cells are not due to the radon exposure but essentially to gamma irradiation. (Author abstract) (23 Refs)

### 21. HEALTH IMPACT OF THE THREE MILE ISLAND ACCIDENT.

**Upton AC, Firebaugh M, Aronson D, Seely S, Maiben W, Penna-Franca E**
**Inst. Environmental Medicine, New York Univ. Medical Center, New York, NY, 10016**
**Ann NY Acad Sci; 365:63-75 1981**

The accident at the Three Mile Island nuclear power plant is discussed with respect to the potential health hazards caused by it. Most of the accidental radiation received by the people living in the area was from xenon-133, xenon-135, and traces of radioactive iodine, mainly 131I. No long-lived fission products were released. The av cumulative dose to people living within 10 miles of the plant was approx 8 mrem, while that to those within 50 miles was approx 1.5 mrem. With respect to cancer, the lifetime risk of less than one additional fatal cancer and less than one additional nonfatal cancer for the population living in a 50 mile radius of the plant, compared with an expectation of 541,000 naturally occurring fatal and nonfatal cancers. Compared with approx 78,000 individuals with genetic defects in the first generation that will naturally occur, less than one offspring of the first and subsequent generations is estimated to have a birth defect attributable to the accident. The potential impact on growth and development of the embryo and fetus is difficult to estimate. While transitory in most persons, the ultimate impact of the effects of the stress caused by the accident remains to be fully assessed. A general discussion of these data is presented. (15 Refs)

### 22. RADIATION AND ROCKY FLATS IN PERSPECTIVE.

**Hunt DC, Crites TR, Lagerquist CR**
**No affiliation given**
**Colo Med; 78(4):111-114 1981**

Plutonium (Pu) and Americium are processed at the Rocky Flats plant near Denver, Colorado. All employees wear dosimetry badges. About 800 workers are exposed to more than background radiation levels. The 180 workers handling Pu were exposed to an av of 875 millirem (mrem)/yr for the last 5 yr; the av was less than 20% of the max permissible exposure level (MPEL: 5,000 mrem/yr). For the other 260 radiation workers, the av was 5.5% of the MPEL (267 mrem/yr). The lifetime lung burden of Pu (8 hr/day, 5 days/wk x 50 yr) is 16 nanoCi (nCi). About 4,000 routine whole-body counts were performed in 1980, including 90 counts after accidental Pu release. Four workers retained measurable amounts of Pu in their lungs (all at less than 10% of the pulmonary MPEL). All injuries that break the skin are measured for x-ray emissions and washed if the count is positive. In 1980, 259 wound counts were obtained; all 14 positive counts became negative after washing. All employees accumulating greater than 50% of the max permissible systemic burden (40 nCi; 26 workers since plant operations began in 1952) are placed on a restricted radioactivity status; 49 others have accumulated 25-50% of the max systemic burden. The procedures used to minimize air, water, and soil radioactivity from the plant are discussed. A typical coal-fired power station, a clay mine, patients given diagnostic or therapeutic radioactive materials, and the background radioactivity of the Front Range of the Rockies emit more radiation than the Rocky Flats plant. The risks of death from lung and bone cancer caused by natural background radiation alone, in the Denver area, are 6,250x and 1,000x greater, respectively, than those expected from plant operations. The area nearest the plant has the same cancer incidence as the area farthest from the plant. The higher rates in the intervening areas are attributable to the normal differences between the center and suburbs of a metropolitan area. (26 Refs)

### 23. ASPECTS OF ENVIRONMENTAL RADIATION AND DOSIMETRY CONCERNING THE HIGH BACKGROUND RADIATION AREA IN CHINA.

**High Background Radiation Research Group**
**(c/o W. Luxin) Lab. Industrial Hygiene, Ministry Public Health, 2 Xinkang Street, Peking, People's Republic of China**
**J Radiat Res (Tokyo); 22(1):88-100 1981**

The study of the health status of residents of Yangjiang County, Guangdong Province, China, an area where the radiation level is about three times that of neighboring areas, is reported. Between 1972 and 1979 no significant difference was observed between high background and control areas with regard to detrimental effects, except perhaps chromosome aberrations. Chemical and gamma-ray spectrometric analyses of the contents of radionuclides in control and high background areas indicated that natural radionuclides were in normal ranges in the former areas while increased by factors of five for uranium and radium and 6-7 for thorium in the latter area. Environmental radiation exposure rates in the high background area fluctuated from 15 to 64 microrads (uR)/hr in the fields, and from 32 to 140 uR/hr in the rooms, as compared with control areas where the values were 5-17 uR/hr in the field and 10-56 uR indoors. The daily intake and localization of radionuclides were determined. 222-Radon and 220-radon activities were determined in exhaled breaths. 228-Radium levels in human teeth were also analyzed. Radiation doses to bone marrow and bone surfaces were estimated. (7 Refs)

### 24. CANCER INCIDENCE IN AN AREA CONTAMINATED WITH RADIONUCLIDES NEAR A NUCLEAR INSTALLATION.

**Johnson CJ**
**42 Hillside Drive, Denver, CO**
**Ambio; 10(4):176-182 1981**

Cancer incidence for 1969-1971 was evaluated in census tracts with and without contamination by plutonium and other radionuclides downwind from the Rocky Flats (nuclear weapons) plant near Denver, Colorado. This area has been exposed to Pu and other radionuclides in the exhaust plumes from the plant since 1953. With reference to unexposed areas 35 km or more from the plant, there was an incidence of cancer in males 24% higher in the area I nearest the plant (3-21 km) and 15% higher in area II, which is 21-29 km from the plant. The corresponding values for females were 10% in area I and 5% in area II. More cases than expected were observed in cancer of the lung, leukemia, lymphoma and myeloma (males only), and tongue, pharynx and esophagus, colon and rectum, liver, pancreas (males only), and only in females for cancer of the gonads, thyroid, and brain. Exposed area II had a correspondingly smaller excess incidence of all cancers, and area III, even further from the plant, had an incidence of all cancer only slightly greater than expected. The classes of cancer found to be in excess were mostly those developing in radiosensitive tissues. Particular attention is given to the remarkably higher incidence of cancer of the testis in the three exposed areas. (58 Refs)

## REVIEWS AND OTHER STUDIES

### 25. EXPERIMENTAL RADIATION CARCINOGENESIS: WHAT HAVE WE LEARNED?

**Fry RJ**
**Biology Div., Oak Ridge Natl. Lab., Oak Ridge, TN, 37830**
**Radiat Res; 87(2):224-239 1981**

The results of animal experiments on radiation carcinogenesis are reviewed with special emphasis on the effects of dose rate, fractionation, and relative biological effectiveness (RBE). Animal models showed that irradiation resulted in an advancement of time of death from tumor without any evidence of an increase in incidence. The variation in dose-response curves reflects the differences and complexities of the mechanisms of carcinogenesis, and the development of techniques which would differentiate the radiation-induced initial events from the exogenous and endogenous factors is of paramount importance. Animal experiments provide useful information on the effect of reduced dose rate on the incidence of tumors. It was shown that the responses to exposures at low dose rate are less than the range of responses to irradiation at high dose rates. The interpolation from data for higher doses of high linear energy transfer (LET) radiation to estimate the risk of lower doses can result in underestimation. The RBE was shown to vary with LET, total dose, dose rate, dose fractionation, and the target tissue. The findings that the susceptibility is related to the natural incidence provide a basis for the quantitative extrapolation of risk estimates from experimental animals to man. (37 Refs)

### 26. INFLUENCE OF NONCARCINOGENIC SECONDARY FACTORS ON RADIATION CARCINOGENESIS.

**Little JB**
**Lab. Radiobiology, Harvard Univ., Sch. Public Health, Boston, MA, 02115**
**Radiat Res; 87(2):240-250 1981**

The results of experiments on the role of secondary factors in the expression of radiation-induced malignant transformation and carcinogenesis are reviewed. Experiments with mouse embryo fibroblasts (C3H 10T1/2 and BALB/3T3 cell lines) showed that approx 13 or 8-9 rounds of cell division were required for transformation to be fully expressed in x-irradiated cells. Delay of subcultivation for 24-48 hr resulted in marked decrease of the transformation frequency. Irradiation of cells with 25 rads followed by exposure to nonmutagenic dose of 12-O-tetradecanoyl-phorbol-13-acetate (active ingredient of croton oil) increased the transformation frequency to the level recorded after irradiation with 200-300 rads. Such agents as saccharin and endogenous epidermal growth factor were also shown to promote malignant transformation in vitro. Incubation of irradiated cells with inhibitors of proteolytic enzymes, vitamin A, or vitamin C was shown to inhibit malignant transformation. These findings suggest that the initial radiation-induced alteration may be a reversible epigenetic event involving an alteration in gene expression. Intratracheal instillations of isotonic saline was shown to increase the frequency of lung cancer in irradiated hamsters (36% compared with 2% in animals subjected to irradiation alone). These findings indicate that the effect of noncarcinogenic secondary factors are not restricted to in vitro transformation systems. (38 Refs)

### 27. BIOLOGICAL EFFECTS OF IONIZING RADIATION AT LOW DOSE AND LOW DOSE RATE.

**Todd P**
**Dept. Microbiology, Cell Biology, Biochemistry and Biophysics, Pennsylvania State Univ., 403 Althouse Lab., University Park, PA, 16802**

**Radiat Res; 87(2):205-207 1981**

The unsolved problems of radiation carcinogenesis at low dose and low dose rate are briefly reviewed. The topics discussed are the linearity of dose-response relationship, effect of fractionated dose of low linear energy transfer radiation, the possibility of comparing human and experimental data for radiation-induced cancer, effect of noncarcinogenic factors, and the epidemiologic data on the existence of a threshold dose for carcinogens in some or any tissues. (2 Refs)

### 28. PUVA CARCINOGENESIS.

**Abel EA**
**No affiliation given**
**Conn Med; 45(6):379 1981**

The data on the carcinogenicity of PUVA therapy (oral administration of 8-methoxypsoralen in combination with longwave UV radiation) currently used for the treatment of recurrent psoriasis a re reviewed. Animal experiments showed high incidence of squamous cell carcinomas and fibrosarcomas after topical, ip or oral administration of large doses of psoralen in combination with UV light. PUVA was found to have a mutagenic effect in bacterial systems. Clinical data indicated a significant increase in the incidence of skin squamous cell carcinoma after an av follow-up period of 2.1 yr. It was recommended that children should not be enrolled in PUVA treatment programs. (4 Refs)

### 29. PREVENTIVE MEDICINE IN THE WORKPLACE - PROSPECTS FOR THE 1980S.

**Upton AC**
**Dept. Environmental Medicine, New York Univ. Medical Center, 550 1st Ave., New York, NY, 10016**
**JOM; 23(8):556-560 1981**

The risks involved with ionizing radiation and carcinogenic agents are an important aspect of occupational health and safety. Determining the safety standards to be set for occupations requires the balancing of the needs of safety with economic and practical needs. Considerable controversy exists about what the risks are and about what standards should be set. Methods used to determine safety standards are discussed. Those dealing with the problem are cautioned against false positive and negative associations and the confounding effects such as socioeconomic factors, previous work history, and nonoccupational factors. (13 Refs)

### 30. INTRODUCTION OF CARCINOGENIC, MUTAGENIC AND TERATOGENIC WORKSHOP (MEETING ABSTRACT).

**Suit HD, Phil D**
**Department of Radiation Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, 02114**
**Long Term Normal Tissue Effects of Cancer Treatment, April 13-15, 1981, Bethesda, Maryland Committe for Radiation Oncology Studies; 1981**

At present the most feared of responses of cells to ionizing radiation, chemotherapeutic agents or combinations thereof are carcinogenesis, mutagenesis or teratogenesis. This concern has increased sharply over the last five to ten yr because of the increasing recognition of the clinical importance of these radiation-induced changes and the fact that substantial numbers of patients are surviving free of their treated tumor for quite long time periods. The discussion of basic mechanism and the observed frequency of these events in cells, tissues, and organisms should assist in focusing our attention on this problem, stimulating additional basic research, and the acquisition of further clinical data. (no Refs)

### 31. THE LOW-LEVEL RADIATION CONTROVERSY REVISITED.

**Barnaby F**
**Stockholm International Peace Res. Inst., Stockholm, Sweden**
**Ambio; 10(4):191-192 1981**

Very little is known about the effects of low levels of radiation. Political and scientific issues involved in the debate about radiation protection are discussed. In general, statistical tests on epidemiological data can show that some dose-response models are incorrect, but they cannot show whic h model is correct. The fundamental mechanisms by which cancers are induced by radiation will probably have to be determined before answers can be elucidated. Molecular and cellular studies are needed to determine the relationship between low-level radiation exposure and cancer. (no Refs)

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# NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

## CHEMICAL CARCINOGENESIS

### 1. THE GENETIC TOXICOLOGY OF ALDRIN AND DIELDRIN.

Ashwood-Smith MJ
Environmental Toxicology Res. Group, Dept. Biology, Univ. Victoria, Victoria, BC V8W 2Y2, Canada
Mutat Res; 86(2):137-154 1981

## RADIATION CARCINOGENESIS

### 2. EFFECTS OF LOW-LEVEL RADIATION ON BIOLOGIC SYSTEMS: A LITERATURE REVIEW.

Best TL, Hoditschek B
Eastern New Mexico Univ., Portales, NM
Effects of Low-Level Radiation on Biologic Systems: A Literature Review. Available from National Technical Information Service, Springfield, VA, as SAND-80-7143:, 246 pp., 1981.

### 3. PHOTOCARCINOGENESIS: AN OVERVIEW.

Forbes PD
Skin and Cancer Hosp., 3322 North Broad St., Philadelphia, PA, 19140
J Invest Dermatol; 77(1):139-143 1981

## DIETARY FACTORS IN CARCINOGENESIS

### 4. EPIDEMIOLOGICAL CORRELATIONS BETWEEN DIET AND CANCER FREQUENCY.

Correa P
Louisiana State Univ. Medical Center, New Orleans, LA, 70112
Cancer Res; 41(9,part2):3685-3689 1981

### 5. ROLE OF DIETARY FIBER IN DIVERTICULAR DISEASE AND COLON CANCER.

Talbot JM
Life Sciences Res. Office, Federation of American Societies for Experimental Biology, Bethesda, MD, 20014
Fed Proc; 40(9):2337-2342 1981

## EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

### 6. PRIMARY HEPATIC CANCER IN ALCOHOLICS.

Tamburro CH, Lee HM
Liver Res. Center, Div. Digestive Diseases and Nutrition, Univ. Louisville Health Sciences Center, 511 South Floyd St., Louisville, KY, 40232
Clin Gastroenterol; 10(2):457-477 1981

### 7. PANCREATIC CANCER AND ALCOHOL.

Okuda K, Ohnishi K
Dept. Medicine, Chiba Univ. Sch. Medicine, 1-8-1 Inohana, Chiba City (280), Japan
Clin Gastroenterol; 10(2):479-484 1981

### 8. HELMINTHS IN THE INDUCTION OF CANCER. II. SCHISTOSOMA HAEMATOBIUM AND BLADDER CANCER.

Schwartz DA
Inst. Medicine, Far Eastern Univ., Manila, Philippines
Trop Geogr Med; 33(1):1-7 1981

### 9. GENETICS OF WILMS'S TUMOR.

Matsunaga E
Dept. Human Genetics, Natl. Inst. Genetics, Mishima, Shizuoka-Ken, 411, Japan
Hum Genet; 57(3):231-246 1981

## CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

### 10. NEOPLASMS: COMPARATIVE PATHOLOGY OF GROWTH IN ANIMALS, PLANTS, AND MAN.

Kaiser HE
Dept. Pathology, Univ. Maryland Sch. Medicine, Baltimore, MD
Neoplasms: Comparative Pathology of Growth in Animals, Plants, and Man. Baltimore, Williams and Wilkins, 908 pp., 1981.

### 11. PULMONARY CARCINOGENESIS: ARYL HYDROCARBON HYDROXYLASE.

McLemore TL, Martin RR
Dept. Medicine, Baylor Coll. Medicine, Houston, TX, 77030
Cancer Treat Res; 1:1-34 1981

### 12. THE GENETIC TOXICITY OF HYDROXYLAMINES.

Marfey P, Robinson E
Dept. Biological Sciences, State Univ. New York at Albany, Albany, NY, 12222
Mutat Res; 86(2):155-191 1981

## MODIFICATION OF CARCINOGENESIS

### 13. MODIFYING FACTORS OF CHEMICAL CARCINOGENESIS.

Beliaev II, Litvinov IuA
Medical Inst., Gorki, USSR
Gig Sanit; (6):59-62 1981
In RUS

### 14. ANTIPROLIFERATIVE EFFECTS OF RETINOIDS RELATED TO THE CELL CYCLE-SPECIFIC INHIBITION OF ORNITHINE DECARBOXYLASE.

Russell DH, Haddox MK
Dept. Pharmacology, Univ. Arizona Coll. Medicine, Tucson, AZ, 85724
Ann NY Acad Sci; 359:281-297 1981

## VIRAL AND IMMUNOLOGICAL ASPECTS OF CARCINOGENESIS

### 15. PATHOGENESIS OF THYMIC LYMPHOMAS IN C57BL MICE.

Boniver J
Laboratoire d'Anatomie Pathologique, Tour de Pathologie B. 23, Universite de Liege au Sart Tilman, 4000 Liege, Belgium
Pathol Res Pract; 171(2):268-278 1981

## METHODOLOGY IN CARCINOGENESIS RESEARCH

### 16. CRITICAL ASSESSMENT OF THE VALUE OF IN VITRO CELL TRANSFORMATION FOR PREDICTING IN VIVO CARCINOGENICITY OF CHEMICALS.

Brookes P
(c/o Lohman, P. H.), Medical Biological Lab. TNO, P.O. Box 45, 2280 AA Rijswijk, The Netherlands
Mutat Res; 86(2):233-242 1981

## OTHER REVIEWS IN CARCINOGENESIS

### 17. MAMMALIAN GENETICS AND CANCER.

Russell ES
Jackson Lab., Bar Harbor, ME, 04609
Prog Clin Biol Res 45: 327 pp., 1981.

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# ICRDB CANCERGRAM

# RADIATION CARCINOGENESIS

SERIES CK06 No. 82/02

FEBRUARY, 1982

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## RADIATION CARCINOGENESIS IN HUMANS

### 1. MALIGNANT MELANOMA AMONG EMPLOYEES OF LAWRENCE LIVERMORE NATIONAL LABORATORY.

**Austin DF, Synder MA, Reynolds PJ, Biggs MW, Stubbs HA**
**Resource for Cancer Epidemiology, State Dept. Health Services, 1450 Broadway, Oakland, CA, 94612**

**Lancet; 2(8249):712-716 1981**

Nineteen cases of malignant melanoma (MM) were observed during 1972-77 among approx 5,100 employees of the Lawrence Livermore National Laboratory, where high energy physics research is conducted. This number was significantly higher (p less than 2 x 10(-6)) than that expected in a compara-

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ble age/race/sex/geographical segment of the population of the San Francisco Bay Area. That excess seemed to occur only among laboratory employees and not among the surrounding community, which suggests that an occupational factor is responsible. Preliminary case-comparison findings suggest that MM risk is not associated with length of employment at the laboratory nor with type of monitored radiation exposure. Although the data did not support an association between MM incidence and all scientific job classifications combined, an excess relative risk was observed among chemists. The reasons for the MM excess have not been identified. (Author abstract) (37 Refs)

### 2. LONG-TERM EFFECTS OF PRENATAL X-RAY OF HUMAN FEMALES. III. MORTALITY AND MORBIDITY.

**Meyer MB, Tonascia J**
**(c/o Tonascia) Dept. Biostatistics, Johns Hopkins Univ. Sch. Hygiene and Public Health, 615 N. Wolfe St., Baltimore, MD, 21205**
**Am J Epidemiol; 114(3):327-336 1981**

Experimental studies and long-term studies of humans exposed to ionizing radiation in utero and after birth show that these exposures increase the risk of cancer in childhood and in later life. A possible life-shortening effect has also been reported. This study followed to their mid-twenties 1,458 women in Baltimore, Maryland, and obtained responses from over 1,100 women in the group. Information about general health and specific diseases was obtained from questionnaires. Deaths were ascertained through family members and death certificates. Mortality rates were slightly higher among exposed than control women, and did not differ by gestational age at the time of exposure. Exposed women reported poor general health significantly more often than controls. Specific diseases occurred similarly in the two groups, although exposed women reported more epilepsy or fits, more ovarian tumors, and more high blood pressure. The strong correlation between wt and high blood pressure and the heavier wt of exposed women seemed to account for this difference. In summary, these matched exposed and control women, followed to their mid-twenties, experienced similar rates of morbidity and mortality. Radiation-induced cancers and life-shortening effects, if any, might not become evident until older ages. (Author abstract) (21 Refs)

## EXPERIMENTAL RADIATION CARCINOGENESIS

### 3. PHOTOCARCINOGENESIS IN HAIRLESS MICE: DOSE-RESPONSE AND THE INFLUENCE OF DOSE-DELIVERY.

**Forbes PD, Blum HF, Davies RE**
**Center for Photobiology, Skin and Cancer Hosp., Temple Univ. Health Sciences Campus, Philadelphia, PA, 19140**
**Photochem Photobiol; 34(3):361-365 1981**

Albino hairless (Skh:HR) mice were exposed to a series of daily (5 days/wk) doses of UV radiation (UVR) from a bank of fluorescent sun lamps (type FS40T12); the 24 animals in each group were examined weekly and skin changes, including tumor locations and sizes, are recorded. Primary endpoints were time to reach a specified proportion of mice bearing one or more tumors, (incidence) and time to reach a specified number of tumors per survivor (tumor yield). By these criteria, the effectiveness of the treatment increased over the range in which the skin could tolerate exposures without exhibiting overt damage (eg ulceration). For the six tolerated daily dose levels, corresponding tumor median latent periods (time to 50% incidence) described a linear relationship with log dose. A second study tested the effect of dose-delivery (time-dose reciprocity). Three groups of animals were treated with a weekly dose, delivered entirely either on 1 day, or one-third on each of 3 days, or one-fifth on each of 5 days, chosen so that the 1-day exposure did not produce overt damage. This weekly dose coincided with the fourth of the six dose levels in the first experiment. Effectiveness of treatment increased directly with the number of fractions per wk. The basis for this dose reciprocity failure is not known, but we expect to investigate the ratio of sublethal to lethal damage in epidermal cells, and to evaluate tumor growth promotion by single vs fractionated exposures. (Author abstract) (16 Refs)

### 4. INHALATION CARCINOGENESIS OF REPEATED EXPOSURES TO HIGH-FIRED 239PUO2 IN RATS.

**Sanders CL, Mahaffey JA**
**Biology Dept., Pacific Northwest Lab., Richland, WA, 99352**
**Health Phys; 41(4):629-644 1981**

Temporal dose-distribution patterns in the lung may be an important factor influencing pulmonary carcinogenesis by inhaled transuranics. This study compared in rats a single exposure to high-fired 239PuO2 particles with repeated inhalation exposures to the same aerosol given either weekly for 9 or 22 wk, or monthly for 3 mo. Prolongation of 239Pu exposure did not significantly change the total pulmonary carcinogenicity of inhaled plutonium. Specific tumor types in some comparisons appeared to be a function of dose rate instead of total radiation dose to the lung. (Author abstract) (10 Refs)

## EFFECTS OF IRRADIATION ON CHROMOSOMES AND DNA

### 5. INDUCTION OF CHROMOSOME ABERRATIONS AND SISTER CHROMATID EXCHANGES BY X RAYS IN DENSITY-INHIBITED CULTURES OF MOUSE 10T1/2 CELLS.

**Nagasawa H, Little JB**
**Lab. Radiobiology, Harvard Univ. Sch. Public Health, Boston, MA, 02115**
**Radiat Res; 87(3):538-551 1981**

The dose-response relationships for the induction of gross chromosomal aberrations and sister chromatid exchanges (SCEs) in density-inhibited cultures of fibroblasts derived from C3H 10T1/2 clone 8 mouse embryo were examined. Changes which occur in cell survival, chromosome aberrations, and SCEs during the repair of potential lethal x-ray damage were also studied. When 10T1/2 cells were irradiated with 200-800 rad in the density-inhibited plateau phase of growth, the cell survival rapidly increased with repair intervals up to 4 hr after x-irradiation; maximal repair occurred after 4-6 hr of delayed subculture. The degree of enhancement of cell survival by potentially lethal damage (PLD) repair was related to the x-ray dose over the range of 200-800 rad. The number of chromosome aberrations decreased progressively when subculture was delayed up to 6 hr after x-irradiation. Thereafter, the aberration frequency remained constant with longer PLD repair periods. There was a mirror image relationship between the increase in cell survival and the reduction in the production of chromosome aberrations. A direct relationship was seen between survival and the prevalence of chromosome aberrations. The change in the induction of SCE during PLD repair showed a more complex pattern. When the cells were subcultured immediately after exposure to 50, 100, and 200 rad of x-rays (no repair), the induction of SCE was increased over baseline (spontaneous) levels in a dose-dependent fashion for doses up to 100 rad with no further increase following 200 rad. When PLD repair was allowed to take place the frequency of SCE induced by 50-200 rad was further enhanced. The dose-response curves for the induction of SCE with PLD repair intervals of 0, 4, and 12 hr after x-irradiation are presented. (26 Refs)

### 6. EARLY POSTRADIATION CHANGES IN CHROMATIN FROM RAT THYMUS: MG++ LEVEL AND INTENSITY OF DEGRADATION AFTER EXPOSURE TO ENDONUCLEASES.

**Chirkova LP, Ermolaeva NV**
**No affiliation given**
**Radiobiologiia; 21(3):335-340 1981**

The changes in the Mg++ content and the rate of chromatin degradation were studied in random-bred and Wistar rats irradiated with 600 R. Animals were sacrificed 0.5, 1, and 2 hr after irradiation, and chromatin specimens isolated from the thymus were subjected to spectrofluorometry. There was a 65-90% increase in the Mg++ content and a 2-3-fold increase in the rate of endonuclease-induced chromatin degradation at pH of 6.4-6.5. (16 Refs) (In RUS)

### 7. FREQUENCY OF CHROMOSOME ABERRATIONS IN HUMAN PERIPHERAL BLOOD LYMPHOCYTES IRRADIATED IN VITRO WITH 60CO GAMMA RAYS AT 1-5 GY AND ANALYZED DURING THE FIRST CELL DIVISION AT DIFFERENT FIXATION TIMES.

**Nugis VIu, Piatkin EK**
**No affiliation given**
**Genetika; 17(6):1117-1125 1981**

The frequency of chromosome aberrations was studied in 50-66-hr cultures of human peripheral blood lymphocytes irradiated in vitro with 60Co gamma rays at 100-500 rads. Sister chromatid staining of the cells in the first division showed that distribution of dicentrics did not depend upon the fixation time. (13 Refs) (In RUS)

## OTHER CELLULAR EFFECTS OF IRRADIATION

### 8. COMPARISON OF SENSITIVITY OF RAD MUTANTS OF DIPLOID YEAST TO HEAT AND GAMMA RADIATION: CELLULAR TARGET FOR HEAT INACTIVATION.

**Reddy NM, Rao BS, Madhvanath U**
**Div. Radiological Protection, Bhabdha Atomic Res. Centre, Trombay, Bombay-400 085, India**
**Int J Radiat Biol; 40(3):235-243 1981**

Wild type and radiation-sensitive mutants rad 53, 54 and 55 of the diploid yeast Saccharomyces cerevisiae, in stationary and log phase were exposed to gamma radiation and hyperthermia (51 C) in order to compare their sensitivity to these agents. The wild type diploid strain exposed to gamma rays showed a sigmoidal survival curve both in stationary and log phase cultures. Log phase cells were significantly more resistant than stationary phase cells. When compared to wild type, the gamma radiation response of the mutants indicated that the mutations in these RAD loci render the cells sensitive in stationary phase and very sensitive in log phase. The response of mutants to hyperthermia was similar to that of wild type cells in both the phases. The log phase cells of both wild type and mutants were more sensitive to heat than stationary phase cells. These results suggest that the RAD loci are not involved in the repair of hyperthermic damage. Since it is known that the products of the RAD genes are involved in the repair of DNA damage, the wild type response of these rad mutants to hyperthermia indicates that the DNA may not be the principal target for hyperthermic killing. Furthermore, the enhanced thermal sensitivity of log phase cells, containing higher amounts of active enzymes and sensitive membrane, strongly suggests that proteins and/or membranes could be the primary targets for thermal inactivation. (Author abstract) (29 Refs)

## THEORETICAL ASPECTS OF RADIATION CARCINOGENESIS

### 9. ON THE QUESTION OF CANCER INDUCTION BY SMALL X-RAY DOSES.

**Webster EW**
**Dept. Radiology, Harvard Medical Sch., Massachusetts General Hosp., Boston, MA, 02114**
**AJR; 137(4):647-666 1981**

There is no proven body of fact that establishes an increase in human cancer after low doses of x or gamma radiation such as those received environmentally, occupationally, or from medical diagnostic procedures; that is, radiation levels below about 10 rad (0.1 Gy). This paper reviews the principal low dose epidemiologic studies that have investigated possible cancer increases. The results of these studies are negative, equivocal, or, when positive, invalidated by methodologic defects or by inconsistency with the feasible carcinogenic effect of background radiation. Despite the lack of direct evidence however, it will never be possible to exclude a very small cancer risk from even the lowest radiation levels, primarily because of statistical limitations in the design of epidemiologic studies. Estimates of cancer risk from low levels of x or gamma ray exposure are therefore based on assumptions regarding the relation between cancer increases and radiation dose. The statistical uncertainties of the meager human data at low doses do not permit unique relations to be established. Nevertheless recent radiobiologic investigations of dose/effect relations for neoplasms in animal populations, for chromosomal damage in human cells, and for malignant transformation in cultured mammalian cell lines suggest that a linear-quadratic relation, when fitted to the human data, provides a reasonable and conservative basis for risk estimation. (Author abstract) (77 Refs)

# ENVIRONMENTAL RADIATION AND PROTECTION STANDARDS

## 10. IODINE-129 IN FORAGE AND DEER ON THE HANFORD SITE AND OTHER PACIFIC NORTHWEST LOCATIONS.

**Price KR, Cadwell LL, Schreckhise RG, Brauer FP**
**Battelle Pacific Northwest Labs., Richland, WA**
**Iodine-129 in Forage and Deer on the Hanford Site and Other Pacific Northwest Locations. Available from National Technical Information Service, Springfield, VA, as PNL-3357:, 34 pp., 1981.**

Samples of surface soil, litter, forage, and deer (rumen content, muscle, liver, and thyroid gland) were collected from Bend, Oregon; Centralia, Washington; Wenatchee, Washington; the Wooten Game Range near Dayton, Washington; and on or near the Hanford Site, Richland, Washington. The concentrations of exp 129 I and exp 127 I were determined using neutron activation techniques. The purpose of the study was to establish the current levels of exp 129 I in the environs of the Hanford Site prior to the proposed restart of fuel reprocessing at the PUREX plant. The results of this study clearly demonstrated the longevity of exp 129 I in the biosphere following gaseous release from a nuclear facility. Analyses of thyroid glands showed that deer living within 160 km (Wooten Game Range) of Hanford had elevated levels of exp 129 I when compared to the more distant Pacific Northwest locations (Centralia, or Bend). Levels of exp 129 I in deer thyroid from Bend, or Centralia, (15 fCi/g wet wt), were about 5x higher than values reported for the central United States, while, Hanford samples were about 2,700x higher. The av concentration of exp 129 I in deer thyroids collected at Hanford in 1978 was similar to samples collected 14 yr earlier. The concentrations of exp 129 I in soil, litter, forage, and other deer samples generally decrease in the order: Hanford greater than Wooten greater than Wenatchee greater than Centralia approx = Bend. This corresponds to an increase in distance from the Hanford Site. (Author abstract)

## 11. URANIUM MILL TAILINGS AND RADON.

**Hanchey LA**
**Sandia Natl. Labs., Albuquerque, NM**
**Uranium Mill Tailings and Radon. Available from National Technical Information Service, Springfield, VA, as SAND-80-2142:, 30 pp., 1981.**

The major health hazard from uranium mill tailings is presumed to be respiratory cancer resulting from the inhalation of radon daughter products. A review of studies on inhalation of radon and its daughters indicates that the hazard from the tailings is extremely small. If the assumptions used in the studies are correct, one or two people per yr in the US may develop cancer as a result of radon exhaled f rom all the Uranium Mill Tailings Remedial Action Program sites. The remedial action should reduce the hazard from the tailings by a factor of about 100. (Author abstract)

## 12. RADIOACTIVITY IN DRINKING WATER.

**Cothern CR**
**Office of Drinking Water, Environmental Protection Agency, Washington, DC**
**Radioactivity in Drinking Water. Available from National Technical Information Service, Springfield, VA, as PB81-192833:, 79 pp., 1981.**

This general overview is designed to assist those involved with public health and drinking water to better understand, interpret and implement EPA's regulation for radioactivity in drinking water. In this presentation the general nuclear properties are shown using naturally occurring isotopes such as radium, radon and uranium as examples. The units of radio-activity (curie, rad and rem) are explained and demonstrated in describing natural radiation; in our surroundings and bodies as well as man-made radiation from medical x-rays, TV, fallout, industrial uses and nuclear power plants and other sources. The health effects discussed include birth defects, genetic damage, cancers, leukemias and others. Several specific examples are given in each disease area as well as their relative importance or rate of occurrence. The risk (in deaths/million people exposed/yr) is tabulated for radioactivity and compared to several other cases including disease, accidents and weather. Possible methods for reducing the radioactivity in drinking water are described. Flow charts are provided that show how to interpret the radiation regulations for drinking water. (Author abstract)

## 13. LONG-TERM EFFECTS OF RADIATION.

**Smith J, Smith T**
**British Medical Journal, London WC1H 9JR, England**
**Br Med J; 283(6296):907-908 1981**

Long-term effects of nuclear war for those not directly attacked stem from delayed fallout. The radiation from such fallout comes from radioactive elements with half-lives of mo or yr, including Cs-137, Sr-89, Sr-90, and C-14. Debris reaching the upper stratosphere would be fairly evenly distributed between the northern and southern hemispheres. Debris not reaching this height would fall out mainly in the hemisphere where the explosion occurred, with a peak deposition at 45 degrees latitude. Deposition would depend on wind patterns and would be heaviest in areas receiving the most rain. The most important isotopes in fallout are Sr-90, which concentrates in bone and is not excreted rapidly, and Cs-137, which is fairly evenly distributed within the body and is excreted over a period of mo. Late effects of brief doses of radiation include cataract formation, leukemia, retarded development of unborn children, and infertility in men. These effects have threshold doses. Cancer and genetic damage do not. Cancer induction would be expected in 5-10% of survivors of an LD50 dose of 450 rads. About half the genetic handicaps produced by radioactive fallout would be expressed in the children or grandchildren of those exposed to radiation. The main threats to survivors of a nuclear war would be non-medical, however. (no Refs)

## 14. MINIMIZING EXCESS RADIOGENIC CANCER DEATHS AFTER A NUCLEAR ATTACK.

**Gant KS, Chester CV**
**Solar and Special Studies Section, Energy Div., Oak Ridge Natl. Lab., Oak Ridge, TN, 37830**
**Health Phys; 41(3):455-463 1981**

An effective civil defense program can reduce prompt fatalities in a nuclear war to a small percentage of the population. Under these circumstances, the number of possible delayed cancer deaths among the survivors due to radiation exposure is of concern. These deaths were estimated for a 5,000-MT attack on a population of the contiguous U.S. which had been 80% evacuated from risk areas and provided with shelters of varying protection factors. Under the assumptions of the study, the principal radiation exposure was from external exposure received in recovery operations outside the shelter during the first yr. Radiogenic cancer deaths were examined by yr of occurrence and age group exposed. Under our assumptions, which include a continuing exposure control program, radiogenic cancer will cause an av loss of life expectancy of less than 1.2 yr. Further evacuation from the most highly contaminated areas, better shelters, and limited daily radiation exposure can reduce the expected cancer effects. If daily exposures of 6 R/day are necessary in recovery operations, the av loss of life expectancy from radiogenic cancer can be lowered to 0.2 yr for the population as a whole by minimizing the exposure of the people under 40 yr old. Use of stored food for the first yr can diminish the impact of ingestion of contaminated food. Radiogenic cancer is unlikely to present any threat to the survival of society in any case, but prudent exposure management can reduce the number of cancer deaths in the yr after the attack. (Author abstract) (19 Refs)

### 15. PERSPECTIVE ON HEALTH EFFECT STUDIES OF LOW-LEVEL EXPOSURE TO RADIATION AND OTHER ENVIRONMENTAL POLLUTANTS.

**Bistline RW**
**Atomics International Div., Rocky Flats Plant, Golden, CO**
**Perspective on Health Effect Studies of Low-Level Exposure to Radiation and Other Environmental Pollutants. Available from National Technical Information Service, Springfield, VA, as RFP-3156:, 3 pp., 1981.**

A perspective view of low-level radiation as a cancer-causing factor is offered. It is concluded that the effects of low-level radiation are so small in relation to the incidence of cancer overall that they are statistically insignificant. (Author abstract)

### 16. DATA ON TMI ACCIDENT DISPUTED.

**Muller HA, MacLeod GK**
**Dept. Health, Commonwealth of Pennsylvania, Harrisburg, PA**
**Pa Med; 84(9):32-33 1981**

Data on the Three Mile Island (TMI) accident that was presented in a preceding article (MacLeod, Pa Med, 84(9): 25-26, 31; 1981) are disputed. Topics discussed include neonatal hypothyroidism, neonatal and infant mortality, the absence of a radiation health unit in Pennsylvania's Department of Health, and problems with the radiation monitoring devices. A rebuttal by the original author is included. (2 Refs)

## REVIEWS AND OTHER STUDIES

### 17. INDUSTRIAL CARCINOGENESIS.

**Vickers CF**
**Dept. Dermatology, Univ. Liverpool, Liverpool L69 3BX, England**
**Br J Dermatol; 105(Suppl21):57-61 1981**

The occurrence of carcinogens in the workplace, particularly as they relate to skin cancers, is reviewed. Such carcinogens include coal, tar, paraffin oil, lubricating oil, pitch, and creosote. Arsenic contamination in the air and water results from metallurgical processe. Arsenic also occurs in dyes, fruit-sprays, glass, and various other materials. X-rays, UV, and other electromagnetic radiation are carcinogenic. Single incidents of trauma can be accepted on a legal basis as carcinogenic, although they are more likely co-carcinogenic. Cutaneous carcinomas seem to require the interaction of a carcinogen and a co-carcinogen, such as UV or trauma, more than do organ-specific carcinomas. The applications of the British system of compensation in cases of exposure to carcinogens is discussed. (14 Refs)

### 18. THE EPIDEMIOLOGY AND PATHOGENESIS OF THE MAMMARY CANCER.

**Pimentei E**
**Catedra de Fisiopatologia, Universidad Central de Venezuela, Caracas, Venezuela**
**Rev Fac Med Univ Cent Venez; 1(1):27-47 1981**

The mammary cancer is five to six times more frequent in the northern countries of Europe and in North America, than in Asia and Africa. The southern European countries and South America are in between. This is a general rule with notable exceptions. In 1978 in Venezuela the total cancer mortality was 13.5%. The mammary cancer was 9.6% of the total women cancer mortality and it was in the fourth place. In the United States the mammary cancer was in the first place with 13.6% of the total women cancer mortality. The pathogenic factors are endogenous (genetic, immunologic, hormonal, reproductive, neural) or exogenous (diet, ionizing irradiation, chemical carcinogens, oncologic viruses). The relative importance of each factor is very variable from one species to another and there are notable differences between various stocks of the same species. The pathogenic factors of human mammary cancer are not well known. The genetic factors seem to be important in the minority of cases. The immunologic and hormonal factors probably are not involved in the transformation of the normal cells, but they influence the growth of neoplastic cells. There are no carcinogenic substances known, which play a role in the origin of the human mamm ary cancer. A minority of cases are related to ionizing irradiation. The possible role of virus is not yet elucidated. (63 Refs) (In SPA)

### 19. SOME RISK FACTORS OF BREAST CANCER.

**Scolozzi R, Salmi R, Coccafogli A, Dell'Acqua G**
**Istituto di Clinical Medica Generale e Terapia Medica, Universita, Ferrara, Italy**
**Recenti Prog Med; 70(5):463-486 1981**

Studies on the risk factors of breast cancer are reviewed. High stature, overweight (obesity), early menarche, hyperestrogenic, reduced fertility, advanced age at first childbirth, short overall duration of lactation, high-caloric, high-fat diet, long-term use of oral contraceptives, especially before the first pregnancy, late menopause, and exposure to ionizing radiation, especially during and shortly after puberty are generally recognized risk factors along with family history of breast cancer. The long-term use of hair dyes, especially of permanent ones, is also considered a risk factor for breast cancer along with other cancers. (134 Refs) (In ITA)

### 20. MECHANISMS OF MALIGNANT GROWTH.

**Grundmann E**
**Pathologisches Institut, Universitat Munster, Domagkstrasse 17, D-4400 Munster, W. Germany**
**Klin Wochenschr; 59(17):931-941 1981**

Analysis of invasive malignancy focuses on the particularly high growth rate of tumor cells, and on the aggressive mechanisms of histolysis favoring the infiltration of the malignant cells into the surrounding tissue. Specific significance is attributed to a certain enzyme directed against Type IV collagen, and to the auto-locomotion of tumor cells, properties that may also explain the highest selective process of metastasization in at least three consecutive steps: Tumor cells invade a blood or lymph vessel, they are transported along blood or lymphatic pathways, and they eventually infiltrate foreign tissue after penetration and destruction of blood or lymph vessel walls. Among the factors involved in the process of metastasization, special interest is due to blood coagulation and to the coexistence of different tumor cell subpopulations within a primary. These features of malignant growth are based on the loss of functional differentiation as manifested eg in the loss of tissue-specific nuclear chromatin structures. Tumor development is triggered by the so-called primary factors which always affect the DNA, ie, the cell genome. Chemical carcinogens, viruses, and shortwave or ionizing irradiation induce DNA defects which, however, can be reversed and mended by special repair mechanisms in most cases. Thus, the actual development and spread of malignancy is ultimately due to deficient repair. Cofactors favoring and promoting carcinogenesis may shorten the latency period, among several other specific chemicals and hormones. Based on current knowledge of tumor dormancy a new concept is proposed for the chronological and morphological sequence of carcinogenesis: Following the development of a primary tumor, certain as yet undefined growth factors and especially immunological factors may be responsible for the development of a progressive tumor disease. (Author abstract) (62 Refs) (In GER)

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## CHEMICAL CARCINOGENESIS

**1. TOXICOLOGICAL ASPECTS OF POLYCYCLIC AROMATIC HYDROCARBONS (PAH).**

De Fernicola NA, De Azevedo FA
Divisao de Toxicologia e Ecotoxicologia, Diretoria de Tecnologia e Desenvolvimento, Sao Paulo, Brazil
Rev Bras Saude Ocup; 33(9):62-68 1981
In POR

**2. EVALUATION OF THE CARCINOGENIC RISK OF CHEMICALS TO HUMANS: SOME ANTINEOPLASTIC AND IMMUNOSUPPRESSIVE AGENTS.**

International Agency for Research on Cancer
International Agency for Res. on Cancer, Lyon, France
IARC Monogr Eval Carcinog Rink Chem Hum; 26:1-411 1981

**3. STUDIES ON THE ROLE OF ORAL CONTRACEPTIVE USE IN THE ETIOLOGY OF BENIGN AND MALIGNANT LIVER TUMORS.**

Mettlin C, Natarajan N
Cancer Control and Epidemiology, Rosewell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
J Surg Oncol; 18(1):73-85 1981

## RADIATION CARCINOGENESIS

**4. EXPERIMENTAL RADIATION CARCINOGENESIS: WHAT HAVE WE LEARNED?**

Fry RJ
Biology Div., Oak Ridge Natl. Lab., Oak Ridge, TN, 37830
Radiat Res; 87(2):224-239 1981

**5. INFLUENCE OF NONCARCINOGENIC SECONDARY FACTORS ON RADIATION CARCINOGENESIS.**

Little JB
Lab. Radiobiology, Harvard Univ., Sch. Public Health, Boston, MA, 02115
Radiat Res; 87(2):240-250 1981

**6. MEDICAL IRRADIATION IN JAPAN - STOCHASTIC RISK ESTIMATION AND ITS REDUCTION.**

Hashizume T
Div. Physics, National Inst. Radiological Sciences, 9-1 Anagawa 4-Chome, Chiba Shi 260, Japan
Nippon Igaku Hoshasen Gakkai Zasshi; 41(5):445-474 1981
In JPN

**7. RADIOACTIVITY IN DRINKING WATER.**

Cothern CR
Office of Drinking Water, Environmental Protection Agency, Washington, DC
Radioactivity in Drinking Water. Available from National Technical Information Service, Springfield, VA, as PB81-192833:, 79 pp., 1981.

## EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

**8. EPIDEMIOLOGY OF GASTROINTESTINAL CANCER.**

Miller AB
NCIC Epidemiology Unit, Univ. Toronto, McMurrich Building, Toronto, Ontario M5S 1A8, Canada
Compr Ther; 7(8):53-58 1981

**9. EPIDEMIOLOGICAL ASPECTS OF ESOPHAGEAL CANCER.**

Ruggieri M, Tosato F, De Rocco K, Lepore M, Cipriano E, Paolini A
IV Cattedra di Clinica Chirurgica Generale e Terapia Chirurgica, Universita degli Studi di Roma, Rome, Italy
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**10. PANCREATIC CANCER.**

Cohn I, Hastings PR
Dept. Surgery, Louisiana State Univ., 1542 Tulane Ave., New Orleans, LA, 70112
UICC Tech Rep Ser. Vol. 57, Issue 12, 142 pp., 1981.

**11. GENETICALLY DETERMINED SUSCEPTIBILITY TO CANCER.**

Marks PA
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Blood; 58(3):415-419 1981

**12. ETIOLOGY, ROLE AND DETECTION OF CHROMOSOMAL ABERRATIONS IN MAN.**

Fabricant JD, Legator MS
Dept. Preventive Medicine, Div. Environmental Toxicology, Univ. Texas Medical Branch, Galveston, TX, 77550
JOM; 23(9):617-625 1981

## ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN CARCINOGENESIS

**13. INDUSTRIAL CARCINOGENESIS.**

Vickers CF
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**14. ENVIRONMENT AND HEALTH (LITERATURE REVIEW).**

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**15. LIFESTYLE AND CANCER.**

Higginson J
International Agency for Res. on Cancer, Lyon, France
Cancer Forum; 5(1):4-14 1981

**16. ASBESTOS, AN ENVIRONMENTAL POLLUTANT.**

Zamfir G, Diaconu R
Institutul de igiena si sanatate publica, Iasi, Romania
Igiena; 30(1):1-9 1981
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**17. REVIEW OF UICC PROGRAM ON SMOKING AND LUNG CANCER.**

Gray N
Smoking and Cancer Program, UICC, 3 rue du Conseil General, 1205 Geneva, Switzerland
Cancer Forum; 5(1):15-18 1981

## CELLULAR AND MOLECUL MECHANISMS IN CARCINO

**18. EXPERIMENTAL APPROAC TOWARDS THE BIOCHEMICAL A S OF CHEMICAL CARCINOGENESIS.**

Laishes BA
McArdle Lab. for Cancer Res., Univ. Wisconsin Medical Sch., Madison, WI, 53706
ACS Symp Ser; 160:197-215 1981

**19. FIBRONECTIN AND RELATED TRANSFORMATION-SENSITIVE CELL SURFACE PROTEINS (ONCOLOGY OVERVIEW).**

International Cancer Research Data Bank
ICRDB Program Office, NCI, Westwood Building, Room 10A18, Bethesda, MD, 20205
Fibronectin and Related Transformation-Sensitive Cell Surface Proteins (Oncology Overview) Chen, L B, ed This Title is Available Through National Technical Information Service, Springfield, VA, as NTISUB/PB81-923001:; OB-81/01:95pp. 1981

**20. PRENEOPLASTIC LESIONS OF THE MAMMARY GLAND. (ONCOLOGY OVERVIEW)**

International Cancer Research Data Bank
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Preneoplastic Lesions of the Mammary Gland (Oncology Overview) Medina, D, ed This Title is Available Through National Technical Information Service, Springfield, VA, as NTISUB/PB81-923002; OB-81/02:134pp. 1981

**21. LYMPHOCYTE DIFFERENTIATION: AN ESSENTIAL BASIS FOR THE COMPREHENSION OF LYMPHOID NEOPLASIA.**

Magrath IT
Pediatric Oncology Branch, Div. Cancer Treatment, NCI, NIH, Public Health Service, United States Dept. Health and Human Services, Bethesda, MD, 20205
JNCI; 67(3):501-514 1981

## MODIFICATION OF CARCINOGENESIS

**22. FACTORS STIMULATING AND INHIBITING TUMOR GROWTH IN CARCINOGENESIS.**

Kochergina NI, Kosova IP
Res. Lab. Experimental Immunobiology, Moscow, USSR
Usp Sovrem Biol; 91(3):409-418 1981
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**23. TWO INDEPENDENT ASPECTS OF TUMOR PROMOTION.**

Berenblum I, Armuth V
Weizmann Inst. Science, Rehovot, Israel
Biochim Biophys Acta; 651(1):51-63 1981

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NCI, Bethesda, MD, 20205
N Engl J Med; 305(13):735-745 1981

**25. REVIEW ARTICLE. REGULATION OF EXPRESSION OF THE INTEGRATED RETROVIRUS GENOME.**

Weinberg RA, Steffen DL
Center for Cancer Res., Massachusetts Inst. Technology, Cambridge, MA, 02139
J Gen Virol; 54(part1):1-8 1981

## METHODOLOGY IN CARCINOGENESIS RESEARCH

**26. THE DEVELOPMENT AND VALIDATION OF MUTAGENICITY SCREENING TESTS.**

Durkin PR, Santodonato J
Center for Chemical Hazard Assessment, Syracuse Res. Corporation, Merill Lane, Syracuse, NY, 13210
Tappi; 64(9):153-159 1981

**27. SHORT-TERM TEST SYSTEMS FOR POTENTIAL MUTAGENS AND CARCINOGENS: I. MICROBIAL TESTS (ONCOLOGY OVERVIEW).**

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Short-Term Test Systems for Potential Mutagens and Carcinogens: I Microbial Test s (Oncology Overview) Simmon, V F; Peirce, V; eds This Title is Available Through National Technical Information Service, Springfield, VA, as NTISUB/PB81-922903:; OK-81/03:124pp. 1981

**28. ANIMAL MODELS OF INTRA-ORAL CHEMICAL CARCINOGENESIS: A REVIEW.**

Eveson JW
Dept. Oral Medicine and Pathology, Guy's Hosp., London SE1 9RT, England
J Oral Pathol; 10(3):129-146 1981

**29. THE CHROMOSOMES IN HEMATOLOGY.**

Berger R
Laboratoire de Cytogenetique, Institut de Recherches sur les Leucemies et les Maladies du Sang, UER d'Hematologie, Hopital Sant-Louis, 2 place du Dr. Fournier, 75475 Paris Cedex 10, France
Cancer Genet Cytogenet; 4(1):69-88 1981

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# ICRDB CANCERGRAM

# RADIATION CARCINOGENESIS

SERIES CK06 No. 82/03

MARCH, 1982

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## RADIATION CARCINOGENESIS IN HUMANS

### 1. CANCER OF THE HEAD AND NECK IN ATOMIC BOMB SURVIVORS: HIROSHIMA AND NAGASAKI, 1957-1976.

**Pinkston JA, Wakabayashi T, Yamamoto T, Asano M, Harada Y, Kumagami H, Takeuchi M**
**Editorial Office, Radiation Effects Res. Foundation, 5-2 Hijiyama Park, Minami-ku, Hiroshima, 730, Japan**
**Cancer; 48(10):2172-2178 1981**

A search was conducted in Hiroshima and Nagasaki for all cases of cancer of the lip, nose and nasal cavity, accessory sinuses, larynx, and the oral cavity and pharynx with their subdi-

HE 20. 3173/2:

visions occurring during the period 1957-1976 among a large, fixed cohort of atomic bomb survivors. A total of 232 cases were identified, of which 154 (66.4%) were histologically confirmed (definite cases). Among definite cases, cancer of the epiglottis and larynx predominated (31.2%), followed by accessory sinus (24.7%) and tongue (18.8%). Of the 154 definite cases, 141 (91.6%) were squamous-cell carcinomas. Only two sarcomas were identified, neither of which was attributable to radiation exposure. Analysis of both total and definite cases, by both total group and major anatomic site, failed to reveal definite evidence of a radiation relationship. Although a suggestive relationship to radiation dose was found for accessory sinus cancers ($p = 0.06$) among the definite cases, inconsistencies in the data do not permit the conclusion that the incidence of tumors in this group increased as a result of atomic bomb radiation exposure. The medical literature concerning post-irradiation head and neck tumors is briefly reviewed. (Author abstract) (39 Refs)

### 2. IMPLICATIONS OF NEW HIROSHIMA AND NAGASAKI DOSE ESTIMATES: CANCER RISKS AND NEUTRON RBE.

**Straume T, Dobson RL**

**Hazards Control Dept., Lawrence Livermore Natl. Lab., P greater than O greater than Box 808, Livermore, CA, 94550**

**Health Phys; 41(4):666-671 1981**

Dose-response relations for radiation-induced leukemia, breast cancer, total malignancies, and chromosome aberrations in atomic bomb survivors were analyzed with the use of new dose estimates that differ substantially from the generally accepted values. They indicate that the gamma ray component and total dose were higher in Hiroshima than previously believed and lower in Nagasaki; neutron components were lower in both cities. Dose-response curves for leukemia and breast cancer were similar in the two cities, but those for total malignancies and chromosome aberrations demonstrated significant inter-city differences. The inter-city differences were due to an increase in neutron relative biological effectiveness (RBE) with decreasing dose due to diminished gamma-ray effectiveness. The neutron RBE for leukemia and breast cancer induction remain to be clarified. (13 Refs)

### 3. REVISED DOSE ESTIMATES AT HIROSHIMA AND NAGASAKI.

**Loewe WE, Mendelsohn E**

**Lawrence Livermore Natl. Lab., P.O. Box 808, Livermore, CA, 94550**

**Health Phys; 41(4):663-666 1981**

New estimates of the neutron and gamma doses at Hiroshima and Nagasaki are presented and compared with the T65D values (1965 tissue dose estimates) for atomic bomb survivors. The revised neutron doses agree closely with cobalt activation measured at 1,180 m from the epicenter in Hiroshima and with total doses measured next to a cold static mock-up of the Hiroshima bomb. No difference between Hiroshima and Nagasaki was found when the Rossi and Mays analysis of leukemia incidence in both cities was repeated with the new data. Results did not support the inference of high neutron relative biological effectiveness values. (10 Refs)

## EXPERIMENTAL RADIATION CARCINOGENESIS

### 4. PRIMARY BONE NEOPLASMS IN BEAGLE DOGS EXPOSED BY INHALATION TO AEROSOLS OF PLUTONIUM-238 DIOXIDE.

**Hahn FF, Mewhinney JA, Merickel BS, Guilmette RA, Boecker BR, McClellan RO**

**Inhalation Toxicology Res. Inst., Lovelace Biomedical and Environmental Res. Inst., Post Office Box 5890, Albuquerque, NM, 87185**

**JNCI; 67(4):917-927 1981**

Primary bone neoplasms developed in beagle dogs briefly exposed by inhalation to aerosols of 238PuO2. 238PuO2 was initially deposited in the respiratory tract where it was retained with a half time greater than 100 days. A portion of the 238Pu was solubilized and translocated to the liver and skeleton. Five yr after exposure, 46 osteosarcomas developed in 35 of 144 exposed dogs. The cumulative absorbed radiation doses to skeleton for these dogs ranged from 210 to 830 rad. Of the 46 bone tumors, 22 originated in the vertebrae, 12 in the humeri, 6 in the pelves, and 6 in miscellaneous long and flat bones. Most of the tumors were well-differentiated sarcomas. Only 10 of the tumors metastasized; the lung was the organ most often invaded. Bone tumors were associated with lesions of radiation osteodysplasia. The number of bone tumors found in this study indicated that inhaled 238PuO2 was an effective skeletal carcinogen. The rate of solubilization in the lung and translocation to bone may be a factor in the radiation dose pattern and type and location of bone tumors that developed after inhalation of 238PuO2. (Author abstract) (18 Refs)

### 5. PLUTONIUM-INDUCED OSTEOSARCOMAS IN THE ST. BERNARD.

**Taylor GN, Thurman GB, Mays CW, Shabestari L, Angus W, Atherton DR**

**Div. Radiobiology, Dept. Pharmacology, Univ. Utah Coll. Medicine, Salt Lake City, UT, 84112**

**Radiat Res; 88(1):180-186 1981**

Factors related to the development of 14 histologically confirmed osteosarcomas in 8/10 St. Bernards injected iv with 239Pu were evaluated. Only 1/14 osteosarcomas arose in the axial skeleton, indicating that the distribution of 239Pu-induced osteosarcomas in St. Bernards more closely resembles that of giant breeds than of beagles (a small breed). For similar injected dosages (uCi/kg), osteosarcomas appeared earlier in St. Bernards than in beagles. For the same time to death, smaller dosages were required for St. Bernards than for beagles. The data indicated that St. Bernards are about 5x more sensitive to osteosarcoma induction than beagles, making St. Bernards about 130x more sensitive than the av person to 239Pu-induced bone sarcomas. Based on this calculation, it was suggested that the St. Bernard may be an excellent experimental model, corresponding to the most susceptible members of the human population, such as those with Paget's disease, who are unusually susceptible to bone cancer. The observed growth rate of the St. Bernards, based on body wt, was much greater than that of beagles. The plasma concentration of somatotropin in St. Bernards was about 1.6x that in beagles of comparable age. Despite these findings, the shorter tumor appearance time in the St. Bernard seemed to be due to its greater radiosensitivity to bone tumor induction, and not due to a faster growth rate of tumor after induction. It was also suggested that the St. Bernard could be useful in evaluating the impact of differences in natural susceptibility on toxicity ratios. (17 Refs)

### 6. THE ROLE OF THYROID HORMONE IN RADIATION AND CHEMICALLY INDUCED ONCOGENESIS (MEETING ABSTRACT).

**Borek C, Guernsey DL, Ong A**

**Department of Radiology, Columbia University, College of Physicians and Surgeons, New York, NY, 10032**

**In Vitro; 17(3):203 1981**

Neoplastic transformation in vitro by x-rays and chemical carcinogens has established the direct oncogenic potential of radiation and chemicals in mammalian cells. Little is known whether hormones, normally present in mammalian serum, can affect this response. Using short-term cultures of diploid hamster embryo cells, and the heteroploid mouse cell line C3H 10T1/2 we studied the effect of triiodothyronine (T3) on transformation. We have found that in both cell types the removal of thyroid hormone from serum-supplemented culture medium (using AG1-X10 resin) inhibits radiation and chemically induced transformation while having no effect on cellular growth rate or survival. When T3 alone is added to thyroid-depleted medium at 10(-7) M, transformation frequency induced by radiation is expressed at a similar frequency as in the presence of culture medium supplemented with untreated serum. We find that exposing the cells to T3 ranging from 10(-11) M to 10(-7) M results in radiation transformation which is dose dependent. Thyroid hormone is essential for the induction and/or expression of x-ray-induced transformations. Recent findings using Benzo-a-pyrene instead of x-rays as the oncogenic agent, indicate that in the absence of T3 there is no transformation and that T3 is required for the induction and/or expression of neoplastic transformation by the chemical carcinogen. (no Refs)

### 7. STRESS AND RADIATION CARCINOGENESIS IN MICE.

**Kalisnik M, Vraspir-Porenta O, Kham-Lindtner T, Logonder-Mlinsek M, Skrk J, Pajntar M**

**Inst. Histology and Embryology, Univ. E. Kardelj Ljubljana, 61105 Ljubljana, Yugoslavia**

**Neoplasma; 28(3):275-279 1981**

In the present experiment irritation consisting of a combination of an optic signal followed by a mild electroshock administered at regular intervals, was started in two groups of animals at the age of 3 mo. At 4 mo of age, one of the irritated and one of the nonirritated groups were exposed to whole-body gamma irradiation at 20 daily doses of 0.5 Gy (50 rad), 1.4 Gy/min (140 rad/min), while the other two groups were sham-irradiated. The animals were autopsied and the specimens were microscopically studied for the presence of malignant tumors. Malignant tumors involving particularly the testes and lungs and leukosis were found in 29% of males, whereas in females the tumor incidence with the mammary, pulmonary and ovarian involvement and leukosis was 39%. The irradiation decreased the minimum latency time in the irritated males and both female groups. In males, the irritation lowered the cumulative prevalence of malignant tumors, a significant decrease being noted at the age of 15 mo. In females, it was increased, with a significant rise observed to occur at the end of the experiment. The opposite effects of irritation on the radiation carcinogenesis in males and females can be attributed to the irradiation-induced specific alterations of the gonads in females and, in part, to a longer survival time observed in the irradiated females. (Author abstract) (12 Refs)

## EXPERIMENTAL RADIATION MUTAGENESIS

### 8. MUTAGENIC AND CYTOTOXIC EVALUATION OF PLUTONIUM-244 (MEETING ABSTRACT).

**Andrews TK, Samuel JE, Frazier ME**

**Biology Department, Pacific Northwest Laboratory, Richland, WA, 99352**

**In Vitro; 17(3):222 1981**

The low specific activity of 244Pu enabled us to conduct a study using in vitro assays to determine the chemical mutagenicity and cytotoxicity of this metal. The effects of this isotope were compared to those of 238Pu and 239Pu to distinguish chemical effects from those caused by radiation. Mutagenicity was determined by the CHO-K1 (Chinese Hamster Ovary) assay, which measures forward mutation of the hypoxanthine-guanine phosphoribosyl transferase (HGPRT) locus. No significant increase in mutation frequency was observed at media concentrations up to 5 ug/ml; however, this isotope was mutagenic at concentrations above 6 ug/ml. A clonal growth assay (VERO), developed at this laboratory, was employed to determine cytotoxicity. As a measure of toxicity, this assay uses the 50% relative plating efficiency concept (RPE 50) ie, concentration of test material that produces a plating efficiency which is 50% of the control value. Concentration-response curves with the VERO growth assay show that 244Pu has an RPE 50 of 0.12 ug/ml, ranking it with the more toxic metals, ie, V greater than Cr greater than Ru greater than 244Pu greater than Cd greater than Hg. (no Refs)

## EFFECTS OF IRRADIATION ON CHROMOSOMES AND DNA

### 9. CHEMICAL CARCINOGENESIS IN THE RAT: COMMON MODE OF ACTION OF CARCINOGENS AT THE CHROMOSOME LEVEL.

**Sugiyama T, Ueda N, Maeda S, Shiraishi N, Goto-Mimura K, Murao S, Chattopadhyay SC**

**Dept. Pathology, Kobe Univ. Sch. Medicine, Chuo-ku, Kobe, Japan 650**

**JNCI; 67(4):831-839 1981**

The chromosomal distribution of chromosome aberrations (CA) and sister chromatid exchanges (SCE) induced by various chemical carcinogens such as 7,12-dimethylbenz[a]anthracene, 7,8,12-trimethylbenz[a]anthracene, 1-butyl-1-nitrosourea, urethan, 4-nitroquinoline 1-oxide, 2-(2-furyl)-3-(5-nitro-2-furyl)acrylamide, and the antineoplastic compound mitomycin C was studied with the use of noninbred Long-Evans male rat bone marrow cells in vivo and in vitro. The CA and SCE induced by these structurally different chemicals were distributed in similar pattern among and along chromosomes when the chemicals were given a short time (6 hr) before the metaphase cells were harvested. The specific distribution pattern of chemically induced CA and SCE along chromosomes was attributed to the late DNA replication of the vulnerable chromosome regions. Conversely, x-ray-induced CA were distributed more randomly. Thus the different chemical carcinogens were shown to exert a similar genetic effect at the chromosome level. (Author abstract) (38 Refs)

### 10. SISTER CHROMATID EXCHANGES (SCE) AND CHROMOSOMAL ABERRATIONS OF CULTURED CELLS OF MOUSE EMBRYO INDUCED BY IONIZING RADIATION AND CHEMICAL CARCINOGEN.

**Piao C, Ge S, Gao F**
**Dept. Biological Effect of Radiation, Lab. Industrial Hygiene, Ministry of Public Health, Beijing, People's Republic of China**
**Acta Anat Sin; 12(2):220-224 1981**

The effects of 60Co-gamma rays and benzopyrene in the induction of SCE and chromosome aberrations are described for cultured murine embryo cells. At a dose level of 300 rad, 60Co-gamma rays induced 1.3 and 24 times more SCE and chromosome aberrations respectively than the unirradiated controls, while a dose of 50 rad produced no difference. At a dose of 0.05 ug per ml of culture media, benzopyrene increased the frequency of SCE by about 1.8 times that of the control while no change in chromosome aberrations was observed. The significance of SCE and chromosome aberrations in the evaluation of carcinogens in discussed. (12 Refs) (In CHI)

### 11. STUDIES ON OSTEOPOROSIS. V - COMPARISON OF METHODS OF EVALUATION OF OSTEOPOROSIS AND STUDY OF CHROMOSOME CHANGES INDUCED BY NEUTRON ACTIVATION.

**Robin JC, Sirianni SR, Pragay DA, Ambrus JL**
**(c/o Ambrus), Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263**
**J Med; 12(4):251-256 1981**

In vivo activation analysis was compared with ashing and atomic absorption spectrophotometry for the determination of total skeletal calcium content in mice. The results were close to identical. The possible mutagenic-carcinogenic effect of repeated exposure to whole body neutron irradiation was studied by chromosome analysis. Under the conditions of these experiments, no significant chromosome changes were seen. (Author abstract) (6 Refs)

## THEORETICAL ASPECTS OF RADIATION CARCINOGENESIS

### 12. SOMATIC MUTATION/NEODIFFERENTIATION/ SELECTION AND THE ORIGINS OF HUMAN CANCERS.

**Lower GM**
**Dept. Veterinary Science, Coll. Agriculture and Life Sciences, Univ. Wisconsin, 1655 Linden Drive, Madison, WI, 53706**
**Med Hypotheses; 7(9):1157-1168 1981**

The etiology of cancer is considered in terms of underlying biological mechanisms: somatic mutation (an alteration in genomic information content) or defective differentiation (alteration in genomic information expression). Human carcinogens, including radiation, chemicals, and viruses or viral components, are discussed. Chemicals have been shown to be responsible for virtually all epithelial cancers. Considering human carcinogenesis to be a multistep procedure, it is possible to accept both hypotheses for the origin of cancer. According to the blocked ontogeny hypothesis of cancer, it is suggested that an agent capable of blocking natural differentiation might bring about a partial or total blockage of natural restraints on proliferation produced by differentiated cells. This theory is discussed in relation to hemoglobinopathies and thalassemias, caused by inherited mutations and genetic deletions that affect the development of Hb production. Others have suggested that most human cancers are not caused by local genomic mutation but are more likely the result of genetic transpositions or rearrangements. It is unknown whether or not or to what extent natural cellular differentiation is mediated by transpositions involving moveable genetic elements. The authors concluded that both genetic transposition and 'autocrine secretion' are within the confines of and consistent with the more general blocked ontogeny hypothesis, and together help provide a plausible mechanism for a somatic mutation/neodifferentiation/ selection theory of human cancer. (51 Refs)

## ENVIRONMENTAL RADIATION AND PROTECTION STANDARDS

### 13. RADIATION LOAD DURING COMPUTER TOMOGRAPHY.

**Stargardt A, Potzschke B**
**Institut fur Rontgendiagnostik, Bereich Medizin der Humboldt-Universitat, Schumannstr. 20/21, DDR-1040 Berlin, E. Germany**
**Radiol Diagn (Berl); 22(3):305-308 1981**

The gonadal and somatic radiation doses and risks of computer tomography were calculated for examinations of the abdomen, thorax, and skull. The radiation dose to the ovaries and testicles was found to be highest during examinations of the urinary bladder and reproductive organs, and lowest during computer tomography of the skull. The risk of cancer or leukemia (per 1,000,000 examinations at a surface dose of 1.4 rads per layer) is highest (38) in the computer tomographic diagnosis of lymphoma, lower during the examination of the abdomen (32), during search for primary tumors (36), and during examination of the urinary bladder region and reproductive organs (28), and lowest during cranial tomography (10). (no Refs) (In GER)

### 14. HEALTH CONSEQUENCES OF ENVIRONMENTAL POLLUTION BY IONIZING RADIATION.

**Kerr CB**
**Commonwealth Inst. Health, Building A27, Univ. Sydney, Sydney, New South Wales 2 006, Australia**
**Med J Aust; 1(13):685-688 1981**

Carcinogenic and mutagenic effects of low-level radiation and risks of further environmental pollution by diagnostic x-rays and the nuclear power industry are discussed. Problems with epidemiologic studies of cancer that is induced by occupational or accidental radiation exposure include the size of the study population and the contribution of background and medical radiation to low-level effects. In a population of one million, an excess of 100 cancer deaths caused by an additional 1 rem (roentgen-equivalent-man) from background radiation would not be detected by current epidemiologic techniques. Animal experiments have shown that ionizing radiation is mutagenic, but no direct evidence exists for radiation-induced genetic damage in humans. The need to protect the public from undue x-ray exposure and the need for more effective radiation protection in uranium mines are noted. (22 Refs)

### 15. THOUSANDS OF CANCER DEATHS AFTER A NUCLEAR MELTDOWN?.

**Trott KR**
**Strahlenbiologisches Institut der Universitat, Bavariaring 19, D-8000 Munchen, W. Germany**
**MMW; 123(39):1428 1981**

A study of the consequences of a nuclear plant meltdown was made. The number of expected cancer deaths from low-level irradiation was calculated as the product of the number of people exposed and the av radiation dose. The risk from low-level radiation was negligible. Therefore all emergency measures should be directed towards people with acute radiation injury. (2 Refs) (In GER)

### 16. POSSIBILITIES TO REDUCE THE RISK OF IRRADIATION DURING MAMMOGRAPHY.

**Zal'tsman IN, Novikova LV**
**Dept. Roentgenology and Radiology, I. M. Sechenov First Medical Inst., Moscow, USSR**
**Vestn Rentgenol Radiol; (4):75-79 1981**

To reduce the radiation load during mass mammography, it was recommended to use a specially designed x-ray apparatus and an amplifying screen, to reduce the number and size of fields, and to estimate the optimal intervals between the repeated examinations. (11 Refs) (In RUS)

## REVIEWS AND OTHER STUDIES

### 17. ETIOLOGICAL AND HISTOPATHOLOGICAL ASPECTS OF THYROID CARCINOMA.

**Bultmann B, Kampshoff E, Heymer B**
**Abt. f. Pathologie der Universitat, Oberer Eselsberg M 23, D-7900 Ulm, W. Germany**
**MMW; 123(37):1353-1357 1981**

Studies on the etiology, epidemiology, and histology of thyroid carcinoma are reviewed. The etiology of thryoid carcinoma is unknown, but hyperthyroidism, struma lymphomatosa, and especially exposure to ionizing radiation during childhood and adolescence are known to be risk factors. Neoplasms can be expected to develop at a frequency of 5-9% after application of 400-1,500 rads. The latent period is 22 yr. About 2/3 of the follicular, 1/3 of the solid, and 1/4 of the papilary carcinomas take up iodine, but the iodine uptake never exceeds that by normal thyroid parenhcyma. Follicular carcinoma accounts for 24%, papillary carcinoma for 41%, medullary carcinoma for 5.3%, anaplastic carcinoma for 21%, and squamous epithelial carcinoma for 0.9% of all thyroid carcinomas. Papillary carcinoma is prevalent in areas without endemic goiter, while follicular carcinoma is prevalent in areas with endemic goiter. The mean survival after diagnosis is only 6.2 mo for anaplastic carcinoma, while the 5-yr survival rates av 34% for medullary carcinoma, 92% for papillary carcinoma, and 85% for follicular carcinoma. (30 Refs) (In GER)

### 18. CHILDHOOD THYROMEGALY: RECENT DEVELOPMENTS.

**Reiter EO, Root AW, Rettig K, Vargas A**
**(c/o Root) Dept. Pediatrics, All Children's Hosp., 801 6th St. South, St. Petersburg, FL, 33701**
**J Pediatr; 99(4):507-518 1981**

Newer aspects of the causes, diagnosis, and management of goiter in the child and adolescent are reviewed. Thyroid immunology is discussed. Etiology and pathogenesis, clinical manifestations, laboratory evaluation, and treatment and prognosis of Hashimoto thyroiditis and Graves disease are presented. Other types of thyromegaly are described. In children, 17-40% of solitary nodules are malignant. A significant association exists between thyroid neoplasms and ionizing radiation to the head and neck. In one study of 2,189 young adults who had irradiation to the tonsils and nasopharynx between 1 and 12 yr of age, nodular disease of the thyroid was present in 713. Thyroid carcinoma was found in 11.2% of these patients. Differential diagnosis of thyroid neoplasms is discussed. Neoplastic lesions are usually discrete. Enlarged metastatic cervical lymph nodes are present in 67-85% of children with thyroid cancer; approx 14% of patients have pulmonary metastases at the time of diagnosis. Thyroid function is usually normal in children with thyroid carcinoma. The presence of a hard, fixed, solid mass (especially in the male), signs of metastasis or invasion (hoarseness, cervical adenopathy), rapid growth of the mass, and a history of irradiation are indications for open surgical biopsy. The combined use of ultrasonography and fine needle aspiration has greatly enhanced diagnostic accuracy and has permitted greater operative selectivity, especially in adults. Surgery, radioiodine ablation, and suppressive doses of thyroid have been employed in the treatment of differentiated thyroid carcinoma. (81 Refs)

### 19. CANCER PREVENTION - PRINCIPLES AND PROBLEMS.

**Schramm T**
**Zentralinstitut fur Krebsforschung, Akademie der Wissenschaften der DDR, Lindenberger Weg 80, 1115 Berlin-Buch, E. Germany**
**Z Aerztl Fortbild (Jena); 75(11/12):526-529 1981**

The general principles, approaches and problems in primary cancer prevention are discussed. The majority of all cancers in humans are caused directly or indirectly by exogenous factors. Th e major causes of cancer include tobacco, alcohol, sunlight, industrial chemicals, radiation, drugs, and possible factors determined by the life style. The existence of threshold doses for carcinogenic factors has not yet been clarified. The individual cancer risk is determined by the interplay of such processes as carcinogenesis, cocarcinogenesis, syncarcinogenesis, and anticarcinogenesis. The possibility of nitrosation of 61 drugs available in East Germany was investigated: slight nitrosation of ethambutol, piperazine, aminophenazone Analgin, desipramine, imipramine, clomipramine, ampicillin, oxacillin, and phenoxymethylpenicillin was determined. It was possible to inhibit but completely suppress the nitrosation of these drugs by the addition of ascorbic acid. (22 Refs) (In GER)

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# NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

## CHEMICAL CARCINOGENESIS

1. CHEMICAL COMPOUNDS AND CANCER RISK.

Schramm T, Janisch W
Zentralinstitut fur Krebsforschung der Akademie der Wissenschaften der DDR, Lind enberger Weg 80, DDR-1115 Berlin, E. Germany
Arch Geschwulstforsch; 51(7):561-565 1981
In GER

2. THE CARCINOGENICITY OF ARSENIC.

Pershagen G
Dept. Environmental Hygeine, Karolinska Inst., Stockholm, Sweden
Environ Health Perspect; 40:93-100 1981

3. THE CARCINOGENICITY OF CHROMIUM.

Norseth T
Inst. Occupational Health, Gydas vei 8, Oslo 3, Norway
Environ Health Perspect; 40:121-130 1981

4. ROLE OF COBALT, IRON, LEAD, MANGANESE, MERCURY, PLATINUM, SELENIUM, AND TITANIUM IN CARCINOGENESIS.

Kazantzis G
TUC Centenary Inst. Occupational Health, London Sch. Hygiene and Tropical Medicine, Keppel St., London WC1E 7HT, England
Environ Health Perspect; 40:143-161 1981

5. RECENT RESEARCH ON NICKEL CARCINOGENESIS.

Sunderman FW
Dept. Lab. Medicine, Univ. Connecticut Sch. Medicine, Farmington, CT, 06032
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# RADIATION CARCINOGENESIS

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**U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES**
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## RADIATION CARCINOGENESIS IN HUMANS

### 1. HABITS OF SUN EXPOSURE AND RISK OF MALIGNANT MELANOMA: AN ANALYSIS OF INCIDENCE RATES IN NORWAY 1955-1977 BY COHORT, SEX, AGE, AND PRIMARY TUMOR SITE.

**Magnus K**
**Cancer Registry Norway, Montebello, Oslo 3, Norway**
**Cancer; 48(10):2329-2335 1981**

Incidence data on malignant melanoma of the skin in Norway from 1955-1977, comprising a total of 5,108 new cases, were analyzed according to cohort, sex, age, and primary tumor site. A continuous increase in incidence of approx 7% per yr was observed for both sexes during the study period. For trunk and lower limb melanomas, the increase and cohort variations in incidence were much greater tha n for face and neck melanoma. A difference between these site groups was also observed in the shape of the cohort curves of age-specific rates. This indicated that the trend in carcinogenic exposure through life was different for the face-neck and the trunk-lower limb. For the generations born 1930-1949, the incidence of malignant melanoma per area unit of skin was greater for the trunk and lower limb than for the face-neck. It is suggested that not only the cumulated dose, but also the intensity of solar radiation may be significant in the cause of malignant melanoma. (Author abstract) (9 Refs)

### 2. A CASE-REFERENT STUDY ON ACUTE MYELOID LEUKEMIA, BACKGROUND RADIATION AND EXPOSURE TO SOLVENTS AND OTHER AGENTS.

**Flodin U, Andersson L, Anjou CG, Palm UB, Vikrot O, Axelson O**
**(c/o Axelson) Dept. Occupational Medicine, Univ. Hosp., S-581 85 Linkoping, Sweden**
**Scand J Work Environ Health; 7(3):169-178 1981**

Cases of 42 persons who died from acute myeloid leukemia (AML) and of 244 referents selected through a procedure providing reasonable homogeneity with respect to age, gender, and domicile were reviewed. Exposure to particular risk factors, especially background radiation and solvents and other agents, was examined. Information on exposure was obtained by questionnaire to the next of kin. The effect of background radiation was assessed with a gamma radiation index which weighed the time spent outdoors and indoors and considered the building material in homes and workplaces of the subjects. Three exposure levels were chosen: category I individuals had a minimal exposure level of less than 4 points, category II had 4 but less than 5 points, and category III had 5 points or more. Between the ages of 20 and 40 yr, to some extent between 50 and 69 yr, but not after 70 yr, an effect from background radiation was noted and a trend suggested an exposure-effect relationship. A six-fold increase in the rate ratio was found with respect to solvent exposure; the effect appeared to modify that of background radiation. Exposure to other etiological agents resulted in relatively modest increases in rate ratio and/or affected very small numbers of persons. Inconclusive results were obtained with respect to prior x-ray exposure because of the low number of studies and small x-ray dosage. The data indicate that in addition to background radiation many other risk factors may operate in the development of leukemia. (34 Refs)

### 3. RADIATION-INDUCED BLADDER CANCER (MEETING ABSTRACT).

**Kennedy DR**
**Royals Women's Hospital, Melbourne, Victoria, Australia**
**Br J Urol; 53(1):74 1981**

A series of patients irradiated for cervical cancer between 1959 and 1969 and followed for 10 to 20 yr is reviewed. Eight hundred and seventy-three patients were treated and of these 331 survived 10 yr or more. In this latter group 4 patients developed a primary bladder carcinoma after a latent period varying between 11 and 16 yr. The annual incidence rate of bladder cancer in the female population is 4.9/100,000. The exposed population at risk is 4905 person yr. Therefore the expected number of cases is 0.240. The observed number is 4 and is 17 x greater than expected. This figure is statistically significant. Hematuria following radiation treatment for carcinoma of the cervix is usually due to vesical telangiectasia. Since it may occasionally be due to a bladder tumor, all such cases should be fully investigated and cystoscopy should be repeated if bleeding recurs. (no Refs)

## EXPERIMENTAL RADIATION CARCINOGENESIS

### 4. RELATIONSHIP BETWEEN FIBRIN CLOT RETRACTION AND TUMORIGENESIS IN C3H/10T1/2 CELLS.

**Azzarone B, Brouty-Boye D, Macieira-Coelho A**
**Dept. de Pathologie Cellulaire, Institut de Cancerologie et d'Immunogenetique, INSERM U 50 and Assoc. Claude-Bernard, 94800 Villejuif, France**
**Int J Cancer; 28(6):799-803 1981**

Fibrin clot retraction (FCR) was studied in C3H/10T1/2 murine fibroblasts. These cells were able to induce FCR with high efficiency during resting phase as well as during active growth. C3H/10T1/2 cells which became tumorigenic after x-irradiation lacked FCR activity. Non-tumorigenic revertant clones regained the capacity to induce FCR, while revertants which progressively back-reverted to the neoplastic state showed intermediate FCR activity. These unstable revertants, when again fully tumorigenic, completely lost FCR activity. (Author abstract) (30 Refs)

### 5. EFFECTS OF DEXAMETHASONE AND CORTISONE WITH X-RAY IRRADIATION ON TRANSFORMATION OF C3H 1OT1/2 CELLS.

**Kennedy AR, Weichselbaum RR**
**Dept. Physiology, Lab. Radiobiology, Harvard Sch. Public Health, Boston, MA, 02115**
**Nature; 293(5836):97-98 1981**

It is reported that dexamethasone (DEX) and cortisone (CORT) do not suppress radiation transformation of C3H 1OT1/2 cells in vitro. DEX (10-7M) or CORT (10-7M) was added to the cultures immediately after irradiation (400 rad of x-rays) and subsequently added at each medium change for the 6-8-wk transformation assay. Dense cell foci were identified and scored as follows: Type 1 were abnormally dense but normal in other respects; Type 2 were large, moderately stellate, and tumorigenic in 60-75% of inoculated mice; and Type 3 were large, highly stellate, and tumorigenic in 80-100% of inoculated mice. The fraction of dishes used that contained Type

3 transformants was 0/40 for controls (no treatment), 12/77 for irradiation alone, 11/78 for CORT alone, 1/78 for DEX alone, 41/76 for irradiation and CORT, and 23/75 for irradiation and DEX. The fractions for cell Types 2 and 3 were 0.40, 26/77, 16/78, 3/78, 54/76, and 34/75, respectively. The results show that for cells exposed to both CORT and x-rays there seemed to be a synergistic response for the induction of malignant transformation. For DEX and x-rays, there was a higher yield of transformants than expected for an additive effect, but it was not significantly greater than the yield of transformants observed for radiation alone or for the expected additive effect of the combined treatments. It is speculated that when clinical efficacy is similar that DEX may give a decreased risk of tumor formation compared with CORT. (19 Refs)

## 6. THE EFFECT OF INTERVAL BETWEEN NEUTRON RADIATION AND DIETHYLSTILBESTROL ON MAMMARY CARCINOGENESIS IN FEMALE ACI RATS (MEETING ABSTRACT).

**Shellabarger CJ, Stone JP, Holtzman S**
**Brookhaven National Laboratory, Upton, NY**
**International Symposium on Health Effects of Tumor Promotion, October 12-15, 1981, Cincinnati, Ohio US Environmental Protection Agency and the American College of Toxicology; 1981**

Both radiation and diethylstilbestrol (DES) are carcinogens for the mammary gland of ACI female rats. When DES is given at about the same time as radiation, DES and radiation interact in a synergistic fashion particularly in regard to the number of mammary adenocarcinomas per rat. We have studied the effect of increasing the time interval between radiation and DES on the capacity of DES to enhance (promote?) radiation-induced mammary carcinogenesis. DES, in the form of a compressed pellet containing a mixture of cholesterol and DES, formulated to av 1.25 mg of DES per 100 g of body wt, was given to groups of approx 28 rats at either 2 days before, or 50, or 100, or 200 days after 0.064 Gray of 0.43 meV neutron radiation. At each time that DES was given to irradiated rats, DES was also given to non-irradiated rats. All rats were studied for 375 days after the date of the DES administration. When the total number of mammary adenocarcinomas was calculated as a percentage of 24 sites per rat at-risk, DES and radiation always produced a response that was larger than the sum of the responses of DES alone plus radiation alone. This result suggests that these two agents can interact in a synergistic fashion. The interaction between radiation and DES did not decline as the time interval between radiation and DES was lengthened. This result suggests that radiation-induced (initiated?) mammary carcinogenesis is not subject to repair since DES enhancement (promotion?) continues to be effective over long time intervals. (no Refs)

## 7. THE INFLUENCE OF CELLULAR PROLIFERATIVE HISTORY ON THE SUSCEPTIBILITY TO ONCOGENIC TRANSFORMATION.

**Chan GL, Little JB**
**Dept. Pathology, Harvard Medical Sch., Sidney Farber Cancer Inst., 44 Binney St., Boston, MA, 02115**
**J Cell Physiol; 109(2):317-322 1981**

Survival and transformation of cells exposed to UV light in the same metabolic state but differing only in their prior proliferative history were studied with C3H mouse embryo-derived 10T/1/2 clone 8 cells. The cells were serially transferred from passage 11 to 15 with 5 x 10(4) cells seeded per 60-mm dish at each passage. One group was passaged as soon as confluence was reached, while two others were kept for 3 or 6 days in confluence at each passage before subculture. There was a progressive selection in all three cases for cells which cloned at higher efficiencies. From passage 11 to 15, there was a slight selection for shorter population doubling times (18.8 hr at passage 10, and 17.0, 17.0, and 17.3 hr at passage 15 after day 0, day 3, and day 6 passage regiments). The saturation densities were 1.1 x 10(6) cells per 60-mm dish at passage 10, and 1.3 x 10(6), 1.2 x 10(6), and 1.1 x 10(6) for the three groups at passage 15, respectively. UV light survival curves for day 0, day 3, and day 6 cells at passage 15 demonstrated slopes of the straight-line portions of-0.32,-0.31, and-0.35 square meter/Joule, respectively. The transformation frequencies for the day 3 and day 6 groups were eight-fold lower than that of the day 0 group. These results suggest that the susceptibility of these cells to transformation is influenced by their proliferative history; intermittent growth quiescence in previous passages decreased this susceptibility. (28 Refs)

## 8. CONVERSION OF HERPETIC LESIONS TO MALIGNANCY BY ULTRAVIOLET EXPOSURE AND PROMOTER APPLICATION.

**Burns JC, Murray BK**
**Dept. Oral Pathology, Dept. Microbiology, Medical Coll. Virginia, Virginia Commonwealth Univ., Richmond, VA, 23298**
**J Gen Virol; 55(part2):305-313 1981**

Many lines of evidence exist associating herpes simplex virus (HSV) with the development of carcinoma, but much of this evidence in anecdotal or associative in nature and does not prove a cause and effect. The purpose of this research was to investigate the oncogenic potential of HSV Type 2 (HSV-2) in vivo. A mouse model for lip carcinogenesis was designed to combine HSV-2 infection, UV exposure and tetradecanoylphorbol-acetate (TPA) application. HSV-2 inoculation on to abraded mouse lips was capable of causing vesicular ulcerative lesions which healed completely after 10 to 14 days. UV irradiation of the HSV lesion site daily for 6 min at 42 ergs/mm2/s on days 3 to 6 post-infection caused hyperkeratosis, acanthosis and dysplasia to develop in several lips; while the same UV exposure by itself failed to alter the histologic appearance. The addition of repeated TPA application to the HSV + UV regimen promoted tumor emergence. Thirty-two of 156 Balb/c mice developed tumors. Although the majority were papillomas, six were squamous cell carcinomas. These tumor-bearing mice had increased HSV-specific antibody titers. HSV antigens were shown to be present in outgrowths from explanted tumors as well as in tumor biopsies by immunoperoxidase staining with HSV-specific antisera. It is suggested that the in vivo UV-irradiated HSV acted as an inducer and TPA as the promoter, analogous to the classical two-stage carcinogenesis model. (Author abstract) (29 Refs)

## 9. CLONAL GROWTH PATTERNS OF GRANULOCYTE PROGENITORS FROM BEAGLE DOGS WITH MYELOID LEUKEMIA (MEETING ABSTRACT).

**Seed TM, Kaspar LV, Tolle DV, Poole CM, Fritz TE**
**Division of Biological and Medical Research, Argonne National Laboratory, Argonne, IL, 60439**
**Exp Hematol; 9(Suppl9):68 1981**

We have extended our knowledge of radiation leukemogenesis by evaluating, in vitro, clonal growth patterns of granulocyte-monocyte progenitors (GM-CFUa) of marrow obtained from 12 cases of canine leukemia induced by protracted low dose (2.5-17 R/day) 60Co gamma irradiation. Growth patterns obtained from the leukemic marrow samples were compared to normal patterns from healthy control dogs and to the patterns obtained from 8 irradiated, nonleukemic dogs bearing solid tumors of both nonhemopoietic and hemopoietic origin. Marrow samples were collected from either the femurs, iliac crests, or ribs, enriched for progenitors, and cultured in soft agar by standard methods. All of the leukemic marrows tested exhibited abnormal clonal growth patterns. The predominant pattern, observed in 10 of the 12 cases was the lawn-type growth; 80% had either no colonies or markedly reduced numbers of colonies (5/10 cases) with less than 7 CFUa/10(5) cells plated, while the remaining 20% had increased numbers of colonies. Phytohemagglutinin-m (PHA-m) incorporated into the culture medium at 20 ug/ml elicited either enhanced colony or enhanced cluster formation in only 1 of 8, and 3 of 8 leukemic marrows tested, respectively. There was no apparent association between myeloid blast cell content in the leukemic marrow specimens and the subsequent level of colony formation observed in either the standard or the PHA-treated cultures. However, the lawn density appeared to be greater in cultures derived from leukemic marrows with high, as opposed to low, myeloid blast cell content. Eight chronically irradiated dogs bearing solid tumors failed to show either the lawn-type growth pattern, or the marked suppression and/or ablation of normal colony formation, seen prominently in the majority in the leukemic marrows studied. (no Refs)

## 10. LIFE-SHORTENING AND CARCINOGENESIS IN MICE IRRADIATED NEONATALLY WITH X-RAYS.

**Sasaki S, Kasuga T**
**Div. Radiation Hazards, Natl. Inst. Radiological Sciences, Chiba 260, Japan**
**Radiat Res; 88(2):313-325 1981**

Modulation of tumor spectrum and dose-dependent relationship for carcinogenesis after x-irradiation of neonatal B6WF1 mice (200, 400, or 600 R within 24 hr of birth) was investigated. Conditions for radiation were 200 kilovolts peak, with a filter of 0.5 mm Cu plus 0.5 mm Al, half-value l ayer of 1.2 mm Cu, and a dose rate of 55-60 R/min. Preweaning death rates in mice irradiated with 200 or 400 R were not significantly different from controls. After 600 R 24% died before weaning. Bone marrow of dead mice was markedly aplastic. Mean and distribution pattern of life spans was affected by irradiation. A very high death rate in the early life of x-irradiated mice was attributable to thymic lymphoma. Incidence of neoplastic disease was high in control mice (71% for females and 60% for males). The number of mice bearing one or more primary neoplasms at autopsy increased in x-irradiated groups except for males that received 200 R. The % of mice dying with multiple primary neoplasms increased in females irradiated with 200 or 400 R. Neoplasms which increased after neonatal irradiation included thymic lymphoma and liver, pituitary and ovarian tumors. Neoplasms decreasing in incidence included lymphoreticular tissue tumors except thymic lymphoma, uterine tumor, and lung tumor in the highest dose group. (25 Refs)

## 11. RADIATION CARCINOGENESIS. COMPREHENSIVE FINAL REPORT, 16 MAY 1979-31 DECEMBER 1980.

**Warren S, Brown CE, Gates O**
**Cancer Res. Inst., New England Deaconess Hosp., Boston, MA**
**Radiation Carcinogenesis. Comprehensive Final Report, 16 May 1979-31 December 1980. Available from National Technical Information Service, Springfield, VA, as DOE/EV/03017-43:, 29 pp., 1981.**

This abstract covers three main areas of investigation: mesothelioma induction by asbestos, radiation tumorigenesis and transplantable tumors. Canadian and Rhodesian asbestos fibers have been administered under anesthesia to rats by intratracheal, intrapleural and ip injection. Additional groups were given 3-methylcholanthrene or x-radiation along with asbestos. A large series of mice also treated as above have displayed mesotheliomas. In addition, glass fiber injections and feeding of asbestos were done and have produced negative results to date. The carcinogenic effect of whole-body radiation on hemi-irradiated parabiont partners exposed to a single 1,000 R dose of x-ray was evidenced by a significant increase in the incidence of malignant tumors in only six tissues: skin, supporting soft tissue, kidney, bone, pancreatic islets and ovary. In the male adrenal medulla and in the female breast genetic and parabiotic hormonal factors were judged to exert a significant effect. The occurrence of incisional (anastomotic) sarcomas in significant numbers in hemi-irradiated and parabiont control pairs suggests the operation of mechanical factors complicating the healing process, only slightly enhanced by radiation. One of the very valuable but unanticipated developments of the rat radiation program was the isolation of two transplantable endocrine tumors with strong hormonal potentials: an insulinoma of the pancreas and a pheo chromocytoma of the adrenal medulla. (Author abstract)

## 12. PRELEUKEMIC CELLS AND RADIATION-INDUCED THYMOMA IN C57B1 MICE (MEETING ABSTRACT).

**Maisin JR, Leonard A, Mattelin G**
**Department of Radiobiology, CEN/SCK, 2400 Mol, Belgium**
**Exp Hematol; 9(Suppl9):185 1981**

It is still uncertain whether tumor cells exist already shortly after a leukemogenic treatment and during the long latent period, or whether they appear only as the tumor develops. A C57Bl strain of mice with 38 chromosomes was, therefore, selected which would allow to detect the presence of preleukemic cells in bone marrow and thymus of irradiated mice. The two substrains of C57Bl mice are histocompatible and have both the H-2b Thy-1b locus. C57Bl/Cnb male mice 4 wk old, were exposed to four weekly doses of 1.75 Gray (Gy) whole body irradiation. Seven, 14, 30, 60 and 90 days after x-ray exposure, 1 x 10(7) bone marrow cells or thymic cells from one animal were injected iv into one C57Bl:Rb(6;15)1Ald mouse whole body exposed to 0.75 or 2 Gy were searched for donor cells in thymus, bone marrow, lymph nodes and spleen of the recipient leukemic mice. If preleukemic cells were present already in the thymus or bone marrow at the time of transplantation, one should eventually find such donor cells in the recipient. The search for such donor cells in thymus, bone marrow, lymph nodes or spleen of the recipients yielded however negative results. In order to study if the absence of preleukemic cells was not due to a minor histoincompatibility between the two substrains of C57Bl mice, bone marrow or thymic cells from one (C57BlCnB x C57Bl:Rb(6;15)1 Ald) F1 mouse with 39 chromosomes irradiated with 4 weekly doses of 1.5 Gy were injected iv into one C57Bl/Cnb mouse with 40 chromosomes irradiated with two or 4 Gy and vice versa. (no Refs)

## 13. INFLUENCE OF SERUM THYMIC FACTOR (F.T.S.) ON RADIATION-INDUCED LEUKAEMOGENESIS IN THYMECTOMIZED AKR MICE (MEETING ABSTRACT).

**Legrand E, Daculsi R, Bach JF, Duplan JF**
**No affiliation given**
**Exp Hematol; 9(Suppl9):67 1981**

The influence of serum thymic factor (FTS) on extra-thymic leukemogenesis induced in thymectomized AKR mice exposed to fractionated sub-lethal irradiation was studied. Thirty day-old thymectomized mice were submitted to 4 weekly doses (1.75 Gray) and thereafter treated with FTS (1 ng) for 9 days. Two groups were restored with either bone marrow (BM) or spleen cells prior to FTS treatment. In another group, mice were treated with FTS (12 ng) for one mo after thymectomy and prior to irradiation. Results indicated that primarily irradiation and FTS, and to lesser extents, restoration and age of the mice at the time of their first radiation exposure influenced leukemogenesis. Irradiation increased the spontaneous low incidence of extra-thymic leukemia up to 50%. Although indication about the expression of endogenous retroviruses in thymectomized AKR is still missing, the possible expression of leukemogenic recombinants either identical to or different from AKR MCF viruses might explain the enhancing effect of radiation in leukemogenesis. Mice developed two types of leukemias: 'null' leukemias whose cells did not bear any detectable theta antigen or surface immunoglobulin and B leukemias. Among the null leukemias, two kinds could be distinguished: 'early' ones which were observed before 450 days, and in which BM and spleen were similarly involved; 'late' ones which displayed the same characteristics as B leukemias ie delayed appearance and splenic origin. Although FTS did not modify the overall frequency of leukemias, it increased significantly the incidence of the 'early' null ones. It had no effect on the frequency nor the latency of late null and B leukemias. Any population of theta negative T cells sensitive to FTS could be an acceptable candidate for 'early' null leukemogenesis. (no Refs)

### 14. CYTOLOGIC FINDINGS IN CARCINOGEN-INDUCED CANINE LUNG TUMORS (MEETING ABSTRACT).

**Yokota S, Pak HY, Teplitz RL, Benfield JR**
**City of Hope National Medical Center, Duarte, CA**
**Acta Cytol (Baltimore); 25(4):455 1981**

Early detection of cancerous lesions of the lung is our ultimate goal and common interest. In order to better evaluate and understand the progression of changes in the development of lung neoplasia, a canine lung cancer animal model has been developed over the past six yr. This model was chosen for several reasons, including lending itself to the same procedural manipulations as used in humans, the feasibility and predictable induction of lung cancer at preselected sites and the rate natural development of lung neoplasms. To date, ten separate protocols using different carcinogens, doses and techniques have been employed. These include: benzo(a)pyrene (BP), nitrosomethyl-urea (NMU), dimethylbenzanthracene (DMBA), methylcholanthrene (MCA) and 91Ybeta radiation. These carcinogens have been introduced by intrabronchial and intrapulmonary sustained release implants of DMBA and 91Ybeta, respectively, and serial intrabronchial submucosal or topical application of aromatic hydrocarbons (BP, DMBA, MCA and NMU). Ten of 89 dogs enrolled in five of the ten protocols have developed lung neoplasms, all of which have been confirmed with histology. This paper describes the cytologic findings of the serial bronchial brushings and washings spanning preinduction of the carcinogens to the development of the lung neoplasms. (no Refs)

## EXPERIMENTAL RADIATION MUTAGENESIS

### 15. DIFFERENTIAL PROTECTIVE EFFECTS OF ANTIOXIDANTS AGAINST CELL KILLING AND MUTAGENESIS OF SALMONELLA TYPHIMURIUM BY GAMMA RADIATION.

**Ben-Hur E, Green M, Prager A, Rosenthal I, Riklis E**
**Nuclear Res. Centre-Negev, P.O. Box 9001, Beer-Sheva, Israel**
**J Radiat Res (Tokyo); 22(2):250-257 1981**

Effects of gamma radiation from a 60Co source on cultures of Salmonella typhimurium were tested in the presence of antioxidants under oxic and anoxic conditions. The commercial mixture G-50 (6% propyl gallate [PG], 14% butylated hydroxytoluene, 8% butylated hydroxyanisole, 36% monoglyceride citrate, and 36% vegetable oil) protected against cell killing and induction of his+ mutations under oxic but not hypoxic conditions. When individual components of G-50 were tested, only PG exerted a protective effect. The amount of protection provided by the mixture was close to that afforded by hypoxia. The protection against cell killing was similar in magnitude to the protection against induction of mutation. No protective effect occurred in oxic cells when antioxidants were added to cells immediately after irradiation. (20 Refs)

### 16. A NOVEL MUTANT OF MOUSE LYMPHOMA CELLS SENSITIVE TO ALKYLATING AGENTS AND CAFFEINE.

**Shiomi T, Hieda-Shiomi N, Sato K**
**Div. Genetics, Natl. Inst. Radiological Sciences, 9-1, Anagawa 4, Chiba 260, Japan**
**Mutat Res; 103(1):61-69 1982**

Sensitivity to physical and chemical mutagens was determined for parental mouse lymphoma L5178Y cells, M10 cells (a N-methyl-N'-nitro-N-nitrosoguanidine sensitive strain), and a novel methyl methanesulfonate [MMS] sensitive strain designated MS-1. The mutagens tested were UV, x-rays, 4-nitroquinoline 1-oxide (4NQO), caffeine, and the alkylating agents MMS, ethyl methanesulfonate (EMS), and mitomycin C (MMC). In terms of the D37 values (doses that reduce cell survival to 37%), M10 cells were 2.5-7x more sensitive to EMS, MMC, 4NQO, MMS, and x-rays than were parental L5178Y cells; the new mutant MS-1 was approx 3x more sensitive to MMS, EMS, MMC, and caffeine than were parental cells. Sensitivity characteristics of M10 cells to x-rays, alkylating agents, and 4NQO resemble some ataxia telangiectasia cells. The sensitivities of MS-1 cells to alkylating agents and caffeine are novel among mammalian cell mutants so far reported. The M10 mutant, which is sensitive to MMS and x-rays but not UV, has been stable for approx 1 yr in continuous culture. The MS-1 mutant has been stable in MMS sensitivity for at least 6 mo in continuous culture. (28 Refs)

### 17. MUTAGENIC EFFECT OF FUROCOUMARIN MONOADDUCTS AND CROSS-LINKS ON BACTERIOPHAGE LAMBDA.

**Belogurov AA, Zavilgelsky GB**
**Inst. Molecular Biology, Acad. Sciences USSR, Moscow, USSR**
**Mutat Res; 84(1):11-15 1981**

The effects of 8-methoxypsoralen and light on bacteriophage lambda were studied. Escherichia coli bacteria were used as hosts. After one irradiation the primary products were monoadducts in DNA. Repeated irradiations formed only cross-links, which had a higher mutagenic effect than monoadducts.

Inactivation of bacteriophage occurred only after multiple irradiations. (14 Refs)

## EFFECTS OF IRRADIATION ON CHROMOSOMES AND DNA

### 18. ABNORMALITIES OF HUMAN CHROMOSOME 13 AND IN VITRO RADIOSENSITIVITY. A STUDY OF 19 FIBROBLAST STRAINS.

**Nove J, Nichols WW, Weichselbaum RR, Little JB**

**(c/o Little) Lab. Radiobiology, Harvard Sch. Public Health, Boston, MA, 02115**

**Mutat Res; 84(1):157-167 1981**

In vitro radiosensitivity was studied in 19 strains of fibroblasts derived from patients with abnormalities of chromosome 13, including 7 with interstitial deletions, 2 with terminal deletions, 4 with complete trisomies, 3 with partial trisomies, 2 with inversions, and 1 with a translocation. Cultures were exposed to at least four doses/culture. Doses ranged from 50 to 900 rads. An unusually wide range of sensitivities (D0: 70-220 rads) was exhibited by the strains. Sensitivities of 132-152 rads had been reported for strains with abnormalities of other autosomes. One strain with complete trisomy of chromosome 13 had the greatest radioresistance reported. Sensitivities of strains bearing deletions distal to locus 13q14 were similar to sensitivities of normal cells. Chromosome 13 apparently is involved in cytotoxicity of x-irradiation. The specific location of this involvement appears to be at 13q14. (27 Refs)

### 19. RADIORESISTANT DNA SYNTHESIS: AN INTRINSIC FEATURE OF ATAXIA TELANGIECTASIA.

**Painter RB**

**Lab. Radiobiology, Univ. California, San Francisco, CA, 94143**

**Mutat Res; 84(1):183-190 1981**

Radioresistance of DNA synthesis (DNAS) was compared in normal human diploid cells of cell line HS27 and six strains derived from patients with ataxia telangiectasia (AT). Three of the AT cell lines had previously been classified as proficient in repair replication after gamma-irradiation. Inhibition of DNAS was measured by incorporation of 14C-thymidine. Cells of normal and AT lines were exposed to 0-5,000 rads of x-rays. To determine the rate of DNAS at various times after irradiation, cultures were pulse-labeled at various times after irradiation. DNAS was strongly inhibited by up to 1,000 rads in HS27, but not in AT cells. DNAS was inhibited to a lesser extent between 1,000 and 5,000 rads in both HS27 and AT cells. In HS27 cells DNAS was reduced to approx 35% of control values for 1 hr, increasing to 60% from 2 to 4 hr after irradiation. In AT cells DNAS was reduced to 75-80% of control values 90 min after irradiation and remained at that level after 4 hr. Inhibition of replicon initiation was the primary factor in radioresistance of AT cells. Chain elongation was also more radioresistant in AT cells than in HS27 cells. Up to 2,000 rads inhibition of DNAS in AT cells was due almost entirely to inhibition of replicon initiation and not of chain elongation. (17 Refs)

### 20. ABNORMAL REGULATION OF DNA REPLICATION AND INCREASED LETHALITY IN ATAXIA TELANGI ECTASIA CELLS EXPOSED TO CARCINOGENIC AGENTS.

**Jaspers NG, De Wit J, Regulski MR, Bootsma D**

**Dept. Cell Biology and Genetics, Erasmus Univ. Rotterdam, Post Office Box 1738, 3000 DR Rotterdam, The Netherlands**

**Cancer Res; 42(1):335-341 1982**

The effect of different carcinogenic agents on the rate of semiconservative DNA replication in normal human and ataxia telangiectasia (AT) cells was investigated. The rate of DNA synthesis in all AT cell strains tested was depressed to a significantly lesser extent than in normal cells after exposure to x-rays under oxia or hypoxia or to bleomycin, agents to which AT cells are hypersensitive. In contrast, inhibition of DNA replication in normal human and AT cells was similar after treatment with some DNA-methylating agents or mitomycin C. Colony-forming ability of AT cells treated with these agents was not different from normal cells. Treatment with 4-nitroquinoline 1-oxide elicited a variable response in both AT and normal cell strains. In some strains, including those shown to be hypersensitive to the drug by other workers, the inhibition of DNA synthesis was more pronounced than in other cell strains, but no significant difference between AT and normal cells could be detected. The rejoining of DNA strand breaks induced by x-rays, measured by DNA elution techniques, occurred within 2 hr after treatment and could not be correlated with the difference in DNA synthesis inhibition in AT and normal cells. After low doses of x-rays, AT cells rejoined single-strand breaks slightly more slowly than did normal cells. The rate of DNA replication in x-irradiated AT and normal cells was not affected by nicotinamide, an inhibitor of poly(adenosine diphosphate ribose) synthesis. These data indicate that the diminished inhibition of DNA replication in carcinogen-treated AT cells (a) is a general characteristic of all AT cell strains, (b) correlates with AT cellular hypersensitivity, (c) is not directly caused by the bulk of the DNA strand breaks produced by carcinogenic agents, and (d) is not based on differences in the induction of poly(adenosine diphosphate ribose) synthesis between x-irradiated AT and normal cells. (Author abstract) (47 Refs)

### 21. CHROMOSOMAL DAMAGE INDUCED BY FUROCOUMARINS AND UVA IN HAMSTER AND HUMAN CELLS INCLUDING CELLS FROM PATIENTS WITH ATAXIA TELANGIECTASIA AND XERODERMA PIGMENTOSUM.

**Natarajan AT, Verdegaal-Immerzeel EA, Ashwood-Smith MJ, Poulton GA**

**Dept. Radiation Genetics and Chemical Mutagenesis, State Univ. Leiden, Wassenaarseweg 72, 2333 AL Leiden, The Netherlands**

**Mutat Res; 84(1):113-124 1981**

The relative capacities of four furocoumarins to sensitize cells to near-UV (UVA) were studied in Chinese hamster ovary cells (CHO) and human cells from normal, ataxia telangiectasia (AT), and xeroderma pigmentosum (XP) individuals. Cells were exposed in vitro to psoralen (PS), 5-methoxypsorale n (5MOP), 8-methoxypsoralen (8MOP), or angelicin (AN) at concentrations of 40 ug/ml. Cultures were irradiated with UVA (320-380 nanometers). In CHO cells the most active substance was PS, followed in order by 8MOP, 5MOP, and AN. The first three produced DNA monoadducts and cross-links, but AN produced only adducts. All four compounds produced higher rates of sister chromatid exchanges (SCE) in AT and XP cells than in normal human cells. AN required high UVA doses to produce damage compared with 8MOP and 5MOP. Normal human cells were approx 2.3 times as sensitive to SCE production than CHO cells. Damage was of the type produced by UV or alkylating agents. Results indicate that 5MOP produces the same effects in human cells as the known carcinogen 8MOP. The use of 5MOP in suntan preparations should therefore not be permitted. (22 Refs)

## 22. THE INFLUENCE OF BIOLOGICAL AND CHEMICAL FACTORS ON THE INDUCTION OF DNA DOUBLE-STRAND BREAKS BY RADIATION (MEETING ABSTRACT).

**Chadwick KH, Leenhouts HP**
**Association Euraton-ITAL, Postbus 48, Wageningen, The Netherlands**
**Int J Radiat Biol; 40(2):260 1981**

One of the problems connected with the association of the DNA double-strand break to the biological effect of radiation and the linear-quadratic dose relationship to the production of DNA double-strand breaks has been the probability that two independently induced single-strand breaks will combine to form a double-strand break. Evidence will be presented which indicates that different chemical species are involved in the induction of the linear and quadratic components of dose-effect relationships. Recent evidence will be presented showing that the immediate linear dose-response curve for double-strand break induction is converted within 3 hr to a linear-quadratic dose-response curve. The combination of this information indicates that both chemical and repair factors are involved in 'lining-up' two independently induced single-strand breaks to produce a double-strand break. (no Refs)

## 23. DNA LESIONS AND CHROMOSOMAL ALTERATIONS (MEETING ABSTRACT).

**Natarajan AT, Van Zeeland AA**
**Laboratory of Radiation Genetics and Chemical Mutagenesis, University of Leiden, Leiden, The Netherlands**
**Int J Radiat Biol; 40(2):205 1981**

Physical and chemical mutagens induce primary lesions in DNA which are subjected to cellular repair. Unrepaired or mis-repaired lesions give rise to chromosomal alterations. The types and frequencies of DNA lesions induced by diverse mutagens are various and it is not clear to which types of lesions lead to chromosomal aberrations. We have examined this question, with regard to the chromosomal aberrations, induced by ionizing radiations and short wave UV, in great detail, by quantifying primary lesions and genetic effects. These studies indicate that the DNA double-strand break is the major lesion responsible for chromosomal aberration induced by ionizing radiations. Pyrimidine dimers seem to be lesions responsible for induction of sister chromatid exchanges, chromosomal aberrations, cell killing as well as point mutations, following short wave UV treatment. (4 Refs)

## 24. CELL-STAGE-SPECIFIC ENHANCEMENT BY CAFFEINE OF THE FREQUENCY OF CHROMATID ABERRATIONS INDUCED BY X-RAYS IN NEURAL GANGLIA OF DROSOPHILA MELANOGASTER.

**De Marco A, Polani S**
**Centro di Genetica Evoluzionistica, C. N. R. presso Istituto di Genetica, Universita di Roma, Rome, Italy**
**Mutat Res; 84(1):91-99 1981**

The effect of caffeine on chromatid aberrations induced by x-rays in neural ganglia of Drosophila melanogaster was studied. Ganglia were removed from third-instar larvae and treated with colchicine (10(-3) M) to accumulate cells in mitosis. They were then exposed to caffeine (10(-2) M), x-rays (500 R), or both. Caffeine alone produced high rates of chromatid aberrations only when added to cells late in G2 phase or during mitotic prophase. Although caffeine alone did not induce aberrations during S-phase, middle G-phase, or C-mitosis, it did enhance the damage produced by x-rays. This enhancement was similar in all three phases. During S- and G2-phases damage consisted primarily of isochromatid deletions and chromatid exchanges. Treatment during C-mitosis produced all types of chromatid damage. Enhancement of X-ray-induced damage may be due to inhibition of DNA repair mechanisms by caffeine. (25 Refs)

## 25. DOSE-RESPONSE RELATIONSHIP FOR INDUCTION OF STRUCTURAL CHROMOSOME ABERRATIONS IN CHINESE HAMSTER OOCYTES AFTER X-IRRADIATION.

**Kamiguchi Y, Mikamo K**

**Dept. Biological Sciences, Asahikawa Medical Coll., 4-5 Nishikagura, Asahikawa 078-11, Japan**

**Mutat Res; 103(1):33-37 1982**

Ovarian sites in normally cycling hamsters were irradiated at 10, 25, 50, 100, 150, 200, and 400 rad when oocytes reached early diakinesis. Percentage of oocytes with structural aberrations increased linearly with increase in dose, reaching nearly 93% in the 400 rad group. Aberration frequency per oocyte increased with dose (from 0.018 in controls to 0.814 in the 200-rad group), showing a dose-response curve fitting the quadratic rather than the linear model. Hamsters in the 400-rad group could not be evaluated because chromosomal damage in irradiated oocytes was too severe to permit determination of the exact number of aberrations. (8 Refs)

## 26. A TRANSIENT POST-IRRADIATION DEFECT IN NEWLY SYNTHESISED DNA.

**Cramp WA, George AM, Lunec J, Harris G, Olsen I, Lewis PD, Chamberlain S, Ahnstrom G, Erixon K**

**MRC Cyclotron Unit, Hammersmith Hosp., London W12 0HS, England**

**Int J Radiat Biol; 40(5):573-579 1981**

Ionizing radiation induced a dose-dependent increase in single-stranded DNA level in radiation-resistant and -sensitive mouse lymphoma cells and in skin fibroblasts from normal donors and Friedreich's ataxia patients. Return to background level occurred without further strand breakage and was interpreted as a rearrangement of the perturbed DNA. (20 Refs)

# OTHER CELLULAR EFFECTS OF

# IRRADIATION

### 27. SURVIVAL CURVES TO GAMMA RAYS OF GLUTATHIONE-DEFICIENT HUMAN FIBROBLASTS INDICATE A REDUCED ENHANCEMENT OF RADIOSENSITIVITY BY OXYGEN AND BY MISONIDAZOLE (MEETING ABSTRACT).

**Deschavanne PJ, Malaise E, Midander J, Revesz L**
**Institut Gustave-Roussy, 94805 Villejuif Cedex, France**
**Conference on Chemical Modification: Radiation and Cytotoxic Drugs, September 17-20, 1981, Key Biscayne, Florida. Committee for Radiation Oncology Studies 139 pp., 1981.**

The fibroblasts deriving from patients suffering from 5-oxoprolinuria are genetically glutathione-synthetase deficient, this deficiency resulting in a dramatic drop of the intracellular level of glutathione (GSH) (6%). The radio-sensitivity of these GSH-deficient fibroblasts has been investigated in vitro using colony forming ability as endpoint; GSH-proficient cells deriving from a healthy brother were used as control. When irradiated in the presence of 95% oxygen -5% CO2, the survival curves were similar. In the presence of 95% air-5% CO2, the GSH-deficient cell line is slightly but significantly more radiosensitive than the proficient one. In oxygen free argon, the survival curve of GSH-deficient cells compared to the oxic survival curve indicates an oxygen enhancement ratio (OER) of 1.5; comparing the survival curves of the control cell line in hypoxic and in oxic conditions, we found an OER of 2.9. When the irradiations were performed in hypoxic conditions in the presence of misonidazole the survival curves were found to be similar for both GSH-deficient and GSH proficient cell lines. It is due to a sensitizing effect higher for GSH-proficient than for GSH-deficient cell line. Cysteamine at a concentration of 20 mM in the culture medium before (30 min) and during the irradiation leads to a protective effect of 1.7 for GSH-deficient and 1.5 for control cell line. These results show that glutathione plays a major role in the response of hypoxic cells to radiations alone or with misonidazole. (no Refs)

### 28. INVOLVEMENT OF A RADIORESISTANT CELL IN THE PRODUCTION OF CIRCULATING INTERFERON INDUCED BY NOCARDIA FRACTIONS IN MICE.

**Barot-Ciorbaru R, Catinot L, Wietzerbin J, Petit JF, Chedid L, Falcoff E**
**Institut de Biochimie, Universite Paris-Sud, Bat. 432, 91405 Orsay, France**
**J Reticuloendothel Soc; 30(4):247-257 1981**

Circulating interferon induction by the immunostimulant Nocardia fractions Nocardia water soluble mitogen (NWSM), Nocardia water soluble mitogen pellet (NWSMP) and peptidoglycan was studied in nude and irradiated mice. The three fractions were active in nude mice, suggesting that cells of thymic origin are not required for interferon synthesis induced by these fractions. NWSM and NWSMP were capable of interferon induction in irradiated mice, but peptidoglycan was inactive. Interferon titers induced by NWSM and NWSMP in irradiated mice were similar to those obtained in normal mice. these results indicate that the cell population (probably macrophages), involved in NWSM- and NWSMP-induced interferon production was radioresistant, whereas the presence of a radiosensitive cell population (probably lymphocytes) was necessary for interferon synthesis induced by peptidoglycan. The antigenic properties and pH stability of interferon induced by the different Nocardia fractions in nude and irradiated mice were examined. The interferon induced by peptidoglycan in nude mice appeared to be related to Type II (now called gamma) interferon. NWSMP, which induced a Type I interferon in normal and nude mice, had the same activity in irradiated mice. NWSM, which contains both NWSMP and peptidoglycan, induced Type I interferon in irradiated mice. NWSM and NWSMP were active interferon inducers in several mouse strains, including endotoxin-resistant C3H/HeJ mice. (Author abstract) (41 Refs)

### 29. THE FIRST TWO MITOTIC CYCLES IN HUMAN LYMPHOCYTES IRRADIATED AT DIFFERENT STAGES.

**Poriadkova NA**
**Res. Inst. Medical Radiology, Obninsk, USSR**
**Radiobiologiia; 21(5):712-715 1981**

The effect of irradiation at different stages of cell division on the kinetics of the mitotic cycle was studied in human peripheral blood lymphocytes. The lymphocytes were irradiated with gamma rays (200 rads) during the G0, late G1, S, and G2 phases; duration of the first mitosis after irradiation was assessed by sister chromatid differential staining technique. Irradiation at G0 did not affect the duration of the first mitosis, irradiation at G1 and S increased the duration 4 hr, and irradiation at G2 increased the duration by 8 hr. (9 Refs) (In RUS)

### 30. DISORDERS OF GLUCOSAMINOGLUCAN METABOLISM AFTER RADIATION INJURY OF THE SKELETON.

**Modiaev VP**
**Res. Inst. Medical Radiology, Obninsk, USSR**
**Med Radiol (Mosk); 26(9):41-43 1981**

Histochemical examination of skeletal and jaw bones of rabbits, guinea pigs, and rats subjected to a whole-body and local gamma irradiation at 100-10,000 rads showed marked inhibition of glucosaminoglucan (GG) metabolism. These findings were indicative of GG radiosensitivity. (18 Refs) (In RUS)

# THEORETICAL ASPECTS OF RADIATION CARCINOGENESIS

### 31. GENERAL MECHANISM FOR THE ORIGIN OF LEUKEMIA (MEETING ABSTRACT).

**Pillow M, Bendix S**
**No affiliation given**
**Tenth International Symposium for Comparative Research on Leukemia and Related Diseases, August 31-September 4, 1981, Los Angeles, California. 187 pp., 1981.**

A postulated mechanism for carcinogenesis is applied to virus-induced leukemia and to leukemia caused by radiation and chemical carcinogens. Malignant disease is postulated to be the result of the uncontrolled and inappropriate expression of developmental gene sequences. This inappropriate expression of developmental sequences can be brought about by DNA mutations, caused by radiation or chemical carcinogens, or by oncogenic viruses, which turn on developmental sequences as a part of their mechanism of making progeny virus. When the expression of embryonic or developmental gene sequences is not controlled, clinical neoplasia is the result. In murine leukemia experiments done by Leiberman and Sachs, certain clones of spontaneous leukemic cells were induced to differentiate by normal macrophage and granulocyte-inducing protein (MGI). Inducible clones had increased production of progeny virus as they differentiated by a factor of five to ten. Those clones which, after the MGI treatment, differentiated into completely mature cells, entirely ceased virus production once they were mature. MGI did not affect virus production in erythroleukemic cells, and erythropoietin did not affect virus production in the myeloid leukemic cells. Studies by Fialkow and others indicate that human leukemia is clonal, and that in the terminal stages of the disease virtually all the blood cells are from the neoplastic clone. Further, these studies show that, at least in chronic myelogenous leukemia, the circulating RBC are from the same clone, but do not show the malignant characteristics. Similarly, in polycythemia vera the WBC from the same neoplastic clone are not themselves malignant. Apparently the initial event leading to malignancy can occur earlier in the developmental pathway than the stage of the proliferating neoplastic cells. Non-malignant cells descend from the same ancestor cell which produced the neoplastic clone. Leukemic transformation seems to relate, in both of these systems, to one or a few developmental steps in a single line of development, even when the original cell in which the lesion occurred was capable of several different lines of development. (2 Refs)

### 32. ON THE MOLECULAR BASIS OF ONCOGENESIS.

**Ahlgren JD**
**Div. Medical Oncology, Vincent T. Lombardi Cancer Res. Center, Georgetown Univ. Sch. Medicine, Washington, DC, 20007**
**J Theor Biol; 93(1):215-223 1981**

A molecular basis for the development of neoplasia is proposed based on viral disruption of genomic regions coding for proteins which control entry into the cell cycle from Go. Such disruption could also be effected by chemically or radiation-induced mutation. Under such conditions normal control proteins would no longer be synthesized. As the available intracellular pool of normal protein is used up, m ore and more cells would remain in the proliferative cycle. Fetal genes might also be derepressed, with a concomitant reduction in the expression of adult genes, resulting in a shift in transformed cells toward a less differentiated state. The expression of derepressed fetal genes would account for observed fetal antigens on tumor cells. The somatic cell destined to form a tumor clone may have multiple abnormal intracellular proteins due to the random nature of simultaneous point mutations in the genome. Endogenous transposable elements may also cleave control cistrons. (35 Refs)

## ENVIRONMENTAL RADIATION AND PROTECTION STANDARDS

### 33. ESTIMATIONS OF POPULATION DOSES AND RISK ESTIMATES FROM OCCUPATIONAL EXPOSURES IN JAPAN, 1978. PART 1. DETERMINATIONS OF ORGAN OR TISSUE DOSES AND EFFECTIVE DOSE EQUIVALENTS.

**Maruyama T, Nishizawa K, Noda Y, Takeda E, Fukuhisa K, Furuya Y, Hashizume T**
**Div. Physics, Nat. Inst. Radiological Sciences, 9-1, Anagawa-4-chome, Chiba-shi 260, Japan**
**J Radiat Res (Tokyo); 22(2):182-203 1981**

A ratio of organ or tissue radiation dose to film-badge reading has been calculated in order to determine effective dose equivalent and population doses. Film-badge readings were collected in a nationwide survey. The ratios for x- and gamma-rays were calculated with a mathematical phantom which simulated the Japanese body and used experimentally determined depth-dose curves. (17 Refs)

### 34. ESTIMATIONS OF POPULATION DOSES AND RISK ESTIMATES FROM OCCUPATIONAL EXPOSURES IN JAPAN, 1978. PART 2. POPULATION DOSES AND RISK ESTIMATES.

**Maruyama T, Nishizawa K, Noda Y, Iwai K, Shiragai A, Furuya Y, Hashizume T**
**Div. Physics, Natl. Inst. Radiological Sciences, 9-1, Anagawa-4-chome, Chiba-shi 260, Japan**
**J Radiat Res (Tokyo); 22(2):204-225 1981**

Population doses and risks of stochastic effects from occupational exposures to external radiation were estimated on the basis of a nationwide survey which involved monitoring film badges for periods of 2 wk, or 0.5 or 1 mo. Various types of doses were estimated using annual collective dose equivalents, av individual dose equivalents, and organ or tissue doses calculated by a previously described method. Annual collective dose equivalents were estimated at approx 6,000 man rem for medical workers, 450 man rem for non-destructive inspection, 450 man rem for industrial non-atomic and 13,300 man rem for nuclear power workers. Population doses (per person/yr) were approx 0.14 millirad (mrad) for the calculated genetically significant dose, 0.15 mrad mean bone marrow dose, 0.14 mrad for the leukemia significant dose, and 0.07 mrad for the malignancy significant dose. Risks of stochastic effects to the individual and to the Japanese population were estimated using the data on annual collective dose equivalent to individual and population doses. Total risk estimate of population is approx 4 persons/yr. Because data include many individuals whose dose equivalent is less than the lower limit estimated by the film badge, overall estimates may be lower than actual exposure. (26 Refs)

### 35. FURTHER 237PU EXPERIMENTS WITH THE PLAICE PLEURONECTES PLATESSA: SUBCELLULAR DISTRIBUTION OF PLUTONIUM IN THE LIVER.

**Leonard DR, Pentreath RJ**
**Directorate Fisheries Res., Fisheries Radiobiological Lab., Hamilton Dock, Lowestoft NR32 1DA, Suffolk, England**
**Marine Biol; 63(1):67-71 1981**

The subcellular distribution of 237Pu in liver of the plaice Pleuronectes platessa was investigated. Locally caught P platessa were injected with 237Pu (0.27 uCi im) and liver homogenates analyzed by differential and isopycnic gradient centrifugation. 237Pu accumulated primarily in the 3,000 and 6,000 g pellets, which by deduction from marker enzyme tests contained both mitochondria and lysosomes. After separation of the fractions, 237Pu was shown to be associated with the lysosome fraction. Metabolism of Pu in the plaice appears similar to that in the rat. (22 Refs)

### 36. PROPOSALS ON USE OF THE BEIR-III REPORT IN ENVIRONMENTAL ASSESSMENTS.

**Cohen BL**
**Univ. Pittsburgh, Pittsburgh, PA, 15260**
**Health Phys; 41(5):769-774 1981**

Procedures to overcome problems associated with the BEIR-III report (NAS80), used as a basis for estimating the cancer risk due to environmental radiation exposure are described. Simple easily utilizable prescriptions for use of BEIR-

III in environmental assessments involving low radiations doses are suggested. Areas considered include whole body low-linear energy transfer (LET) radiation, low-LET radiation to specific organs, whole body exposure to neutrons, and alpha particle exposure to particular organs. (Author abstract) (8 Refs)

### 37. INTERNAL RESEARCH AND STANDARD SETTING.

**Stannard JN**
**Dept. Community Medicine, Univ. California, San Diego-La Jolla, CA**
**Health Phys; 41(5):703-708 1981**

The development of internal emitter standards by the International Commission on Radiological Protection and the National Council on Radiation Protection is described. Standards were developed for uranium and plutonium based on nephrotoxic and radiation effects as well as comparison to other radioactive elements. A reference man, lung, and gastrointestinal models were devised. (14 Refs)

### 38. TECHNICAL BASES FOR ESTIMATING FISSION PRODUCT BEHAVIOR DURING LWR ACCIDENTS.

**Nuclear Regulatory Commission**
**Nuclear Regulatory Commission, Washington, DC**
**Technical Bases for Estimating Fission Product Behavior During LWR Accidents. Available from National Technical Information Service, Springfield, VA, as NUREG-0772:, 343 pp., 1981.**

The objective of this report is to provide the Nuclear Regulatory Commission and the public with a description of the best technical information currently available for estimating the release of radioactive material during postulated reactor accidents, and to identify where gaps exist in our knowledge. This report focuses on those low probability-high consequence accidents involving severe damage to the reactor core and core meltdown that dominate the risk to the public. Furthermore, in this report particular emphasis is placed on the accident behavior of radioactive iodine, as (1) radioiodine is predicted to be a major contributor to public exposure, (2) current regulatory accident analysis procedures focus on iodine, and (3) several technical issues have been raised recently about the magnitude of iodine release. The generation, transport, and attenuation of aerosols were also investigated in some detail to assess their effect on fission product release estimates and to determine the performance of engineered safety features under accident conditions exceeding their design bases. (Author abstract)

### 39. THE GASTROINTESTINAL ABSORPTION OF PLUTONIUM IN THE HAMSTER AFTER INGESTION AT LOW CONCENTRATIONS IN DRINKING WATER.

**Stather JW, Harrison JD, David AJ, Sumner SA**
**Natl. Radiological Protection Board, Harwell, Didcot, Oxon OX11 0RQ, England**
**Health Phys; 41(5):780-783 1981**

The results of this study in hamsters indicate that the ingestion of very small quantities of plutonium in drinking water will not lead to levels of absorption above the value of 0.01% adopted by the ICRP for soluble forms of plutonium (ICRP79). The values of 0.001-0.003% absorption obtained for plutonium in drinking water at a concentration of about 1.5 x 10(-13) g ml-1 showed that neither the presence of Pu(VI) nor the low concentration resulted in enhanced uptake. (Author abstract) (13 Refs)

### 40. CHARACTERISTICS OF THE RISK OF INTERNAL CONTAMINATION OF THE HUMAN BODY IN WORKERS EMPLOYED IN RADIOISOTOPE LABORATORIES IN POLAND.

**Adamiak-Ziemba J, Domanski T, Doniec J**
**Zaklad Ochrony Radiologicznej, Instytut Medycyny Pracy, ul. Teresy 8, 90-950 Lodz, Poland**
**Pol Tyg Lek; 36(31):1201-1204 1981**

The risk of internal contamination with radioactive isotopes was surveyed in isotope laboratories in Poland. A total of 1,987 employees were found to be exposed to radioactive isotopes in 247 radiological laboratories using open radiation sources. Many employees were found to be exposed to several (up to 17) isotopes. Most employees were exposed to tritium (over 500 employees), 125I, 131I, 32P, 51Cr and 99mTc (over 100); all these isotopes belong to the radiotoxicity Class II, III, and IV. Only 52 employees were exposed to 226Ra (radiotoxicity Class I). (6 Refs) (In POL)

## REVIEWS AND OTHER STUDIES

### 41. INCREASED RISK OF LEUKEMIA IN POLYCYTHEMIA VERA PATIENTS TREATED WITH CHLORAMBUC IL.

**Caspary WF, Heimpel H, Von Heyden H**
**Hanau, W. Germany**
**Inn Med; 8(5):209-212 1981**

Previously published results of a prospective, randomized, controlled clinical study (N Engl J Med 304: 441, 1980) concerning the treatment of patients with polycythemia vera (PV) are summarized by Caspary and discussed by Heimpel and by von Heiden. It is noted that the results indicated that the use of chlorambucil in the treatment of PV increased the rate of development of PV into acute leukemia. Definition, symptoms, and diagnosis of PV are considered, with emphasis on hematologic findings. Conventional treatment of PV by surgery or radioactive phosphorus is compared with newer treatments involving the use of myelosuppressive drugs. The danger of acute leukemia development associated with the use of either the radiologic or chemotherapeutic method is discussed. A series of studies designed to identify the optimal treatment for PV are briefly described. Indications and contraindications are listed for the use of the surgical, radiologic, and myelosuppressive treatment of patients with PV. (10 Refs) (In GER)

### 42. SETTING THE RECORDS STRAIGHT: THE NEED FOR A CENTRAL REGISTRY OF MEDICAL-DENTAL RADIATION EXPOSURE.

**Kreisler L, Freidrichs RE**
**Reynolds Electrical and Engineering Co. Inc., Las Vegas, NV**
**Appl Radiol; 10(6):93-98 1981**

The need for record keeping of a person's accumulated dose of ionizing radiation (IR) recieved from medical and dental procedures (MDP) is discussed. Known adverse effects of radiation in humans, occupational and nonoccupational exposures considered safe, and radiation exposure associated with various MDP are reviewed. Documented adverse effects discussed relate to genetics, prenatal x-radiation, polycythemia vera, thyroid cancer, thyrotoxicosis, pneumothorax for tuberculosis, radiologic practice, dentistry, laboratory and other occupational exposure (OE), head and neck irradiation, ankylosing spondylitis (AS), Nagasaki and Hiroshima survivors, radium dial painters, thorotrast studies (liver examination), uranium miners, weapons testing, treatment of tuberculosis and AS with preparation containing 224Ra, and pelvic irradiation. Additional restrictions on OE may be imposed by the United States Nuclear Regulatory Commission. Highest doses of IR result from the use of radionuclides in nuclear medicine.

## 43. EPIDEMIOLOGY OF PITUITARY ADENOMAS.

**Gold EB**

**Dept. Epidemiology, Sch. Hygiene and Public Health, Johns Hopkins Univ., 615 Wolfe St., Baltimore, MD, 21205**

**Epidemiol Rev; 3:163-183 1981**

Epidemiologic data, methodological problems associated with study of epidemiologic characteristics, and causal factors for pituitary adenomas are reviewed. Clinical features and treatment of pituitary adenomas are summarized. Incidence and prevalence are presented with respect to age, pituitar y tumors in children and adolescents, time trends, sex differences, geographic variations, and multiple endocrine adenomatosis syndrome Type I. Exogenous risk factors presented are radiation, chemical carcinogens, estrogens, and oral contraceptives. Included are analyses of pituitary tumors as a proportion of all CNS neoplasms from selected studies, male:female ratios of incidence rates of pituitary tumors from selected reports, pituitary adenomas as a proportion of all primary CNS neoplasms from selected countries, av annual incidence rates/100,000 population for pituitary adenomas from selected countries, effects of diet, I131, and x-rays on induction of pituitary tumors in mice, incidence rate of pituitary tumors in female mice following total body neutron- and x-radiation, and frequency of pituitary adenomas in women with postpill vs non-postpill amenorrhea or amenorrhea-galactorrhea from selected reports. (154 Refs)

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## 44. PERSPECTIVES IN THE EPIDEMIOLOGY OF MELANOMA (MEETING ABSTRACT).

**van der Esch EP, Stukonis MK**
**Antoni van Leeuwenhoekziekenhuis, Amsterdam, The Netherlands**
**W.H.O. Seminar on Malignant Melanoma, June 24, 1981, Gothenburg, Sweden. World Health Organization 35 pp., 1981.**

UV irradiation appears to be a factor in the carcinogenesis of melanoma for the fair skinned population. Is an association with other factors existing? A very low correlation was found with sunlight related sites of cancer such as lips and skin. The correlation is strong for females with ovarian cancer. The aim of the study is to indicate methods for investigations exploring the apparently inconsistent findings. The melanoma incidence of three areas has been analyzed for the functions of age, sex and sites. Concluding that the genesis of melanoma is also determined by endogenous host factors, further research should include: a) Population-based registration of melanoma for cohort studies, studies on migrant populations and populations characterized by their way of life. b) Studies on correlation with other malignancies, with avoidable circumstantial factors and with endogenic factors. c) Case-control studies should complement the studies to define attributable risks. Exposed and non-exposed anatomical sites should be considered separately for incidental overdose and cumulative effects of prolonged exposure. (no Refs)

## 45. CLINICAL MANIFESTATIONS AND PATHOGENESIS OF ACUTE LESIONS CAUSED BY PRODUCTS OF NUCLEAR FISSION.

**Vasilenko Ila**
**No affiliation given**
**Med Radiol (Mosk); 26(9):75-83 1981**

The mechanism of toxic and carcinogenic effects of products of nuclear fission (PNF) is reviewed. Exposure to PNF produces acute metabolic, hematological, and immunological disorders. The most pronounced changes are observed after exposure by inhalation. The long-term effects of PNF include development of benign and malignant neoplasms, primarily in the endocrine organs. (37 Refs) (In RUS)

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As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

## DIETARY FACTORS IN CARCINOGENESIS

1. NUTRITION AND ENVIRONMENTAL HEALTH: THE INFLUENCE OF NUTRITIONAL STATUS ON POLLUTANT TOXICITY AND CARCINOGENICITY. VOLUME 2: MINERALS AND MACRONUTRIENTS.

Calabrese EJ

Environmental Health Program, Div. Public Health, Univ. Massachusetts, Amherst, MA

Nutrition and Environmental Health: The Influence of Nutritional Status on Pollutant Toxicity and Carcinogenicity. Volume 2: Minerals and Macronutrients. New York, John Wiley and Sons, 468 pp., 1981.

## EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

2. RETROSPECT AND PROSPECT OF STUDIES ON DIGESTIVE SYSTEM DISEASES IN CHINA.

Zhang X

Dept. Internal Medicine, Capital Hosp., Chinese Acad. Medical Sciences, Beijing, People's Republic of China

Zhonghua Xiaohua Zazhi; 1(1):1-4 1981

In CHI

3. EPIDEMIOLOGY OF PITUITARY ADENOMAS.

Gold EB

Dept. Epidemiology, Sch. Hygiene and Public Health, Johns Hopkins Univ., 615 Wolfe St., Baltimore, MD, 21205

Epidemiol Rev; 3:163-183 1981

4. BLADDER CANCER EPIDEMIOLOGY.

Matanoski GM, Elliott EA

Dept. Epidemiology, Sch. Hygiene and Public Health, Johns Hopkins Univ., 615 North Wolfe St., Baltimore, MD, 21205

Epidemiol Rev; 3:203-229 1981

5. THE EPIDEMIOLOGY OF BENIGN BREAST DISEASE.

Ernster VL

Dept. Epidemiology and International Health, 1699HSW, Univ. California, San Francisco, CA, 94143

Epidemiol Rev; 3:184-202 1981

## ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN CARCINOGENESIS

6. AIR POLLUTION AND BIOLOGICAL DEFENCE.

Schlipkoter HW, Dolgner R

Med. Institut fur Umwelthygiene an der Univ., Gurlittstrasse 53, D-4000 Dusseldorf 1, W. Germany

Zentralbl Bakteriol [Orig A]; 172(4/5):299-311 1981

In GER

7. CANCER AND THE PHYSICOCHEMICAL QUALITY OF DRINKING WATER IN QUEBEC.

Thouez JP, Beauchamp Y, Simard A

Dept. Geography, Univ. Montreal, Montreal, Quebec, Canada

Soc Sci Med [Med Geogr]; 15(1):213-223 1981

## VIRAL AND IMMUNOLOGICAL ASPECTS OF CARCINOGENESIS

8. ONCOGENIC VIRUSES.

Wyke JA

Imperial Cancer Res. Fund, P.O. Box 123, Lincoln's Inn Fields, London WC2A 3PX, England

J Pathol; 135(1):39-85 1981

9. ROLE OF VIRUSES IN THE ETIOLOGY OF NATURALLY OCCURRING FELINE LEUKEMIA.

Essex M, Grant CK, Cotter SM, Hardy Jr WD

Dept. Microbiology, Harvard Sch. Public Health, 665 Huntington Ave., Boston, MA, 02115

Haematol Blood Transfus; 26:483-487 1981

## METHODOLOGY IN CARCINOGENESIS RESEARCH

10. MAMMALIAN IN VIVO AND IN VITRO CYTOGENETIC ASAYS: A REPORT OF THE U.S. EPA'S GENE-TOX PROGRAM.

Preston RJ, Au W, Bender MA, Brewen JG, Carrano AV, Heddle JA, McFee AF, Wolff S, Wassom JS

Biology Div., Oak Ridge Natl. Lab., Oak Ridge, TN, 37830

Mutat Res; 87(2):143-188 1981

11. BACTERIAL SYSTEMS FOR CARCINOGENICITY TESTING.

Mohn GR

Dept. Radiation Genetics and Chemical Mutagenesis, State Univ. Leiden, Wassenaarseweg 72, 2333 AL Leiden, The Netherlands

Mutat Res; 87(2):191-210 1981

12. MUTAGENESIS BY CHEMICAL AGENTS IN V79 CHINESE HAMSTER CELLS: A REVIEW AND ANALYSIS OF THE LITERATURE.

Bradley MO, Bhuyan B, Francis MC, Langenbach R, Peterson A, Huberman E

Merck Inst. for Therapeutic Res., West Point, PA, 19486

Mutat Res; 87(2):81-142 1981

## OTHER REVIEWS IN CARCINOGENESIS

13. CANCER BIOLOGY.

Ruddon RW

Biological Markers Program, NCI-Frederick Cancer Res. Center, Frederick, MD

Cancer Biology. New York, Oxford University Press, 344 pp., 1981.

14. AVOIDABLE CANCER: ATTRIBUTION OF RISK.

Doll R

Radcliffe Infirmary, Oxford, England

S Afr Cancer Bull; 25(3):125-146 1981

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# RADIATION CARCINOGENESIS

SERIES CK06 No. 82/05

MAY, 1982

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## RADIATION CARCINOGENESIS IN HUMANS

### 1. CARCINOGENIC, MUTAGENIC, TERATOGENIC WORKSHOP.

**Suit H, Hall E, Frei E**
**Dept. Radiation Medicine, Massachusetts General Hosp., Boston, MA, 02114**
**Cancer Clin Trials; 4(Suppl):37-41 1981**

Studies on the incidence of tumors attributed to radiation and chemotherapy are reviewed. An analysis of 106,074 patients receiving radiation therapy between 1958 and 1980 re-

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vealed 30 sarcomas which had developed within the irradiated tissue. The median lag period was 10 yr. Of the 30 patients, seven were alive 1.5-20 yr after treatment of the 'radiation-induced' tumor. In patients treated for ovarian carcinoma by alkylating agents, a 15-fold increase in the risk of acute myelogenous leukemia has been re ported. Among 438 patients treated for Hodgkin's disease, the observed to expected ratio of leukemia was 3.8 for patients treated with total nodal or extended field radiation therapy, 3.2 for chemotherapy, 23 for extensive radiation and chemotherapy, and 1.6 for local field irradiation. In another study of leukemic development among 1,096 patients treated for Hodgkin's disease, the incidence was 0/417, radiation alone; 12/453, radiation and chemotherapy; 1/124, radiation failure followed by chemotherapy; and 2/37, chemotherapy only. The importance of considering the carcinogenicity of chemotherapeutic agents in future clinical trials is stressed. Models of carcinogenesis include various interpretations of the role of the processes of initiation and promotion. Problems of extrapolation of carcinogenic findings from one model system do another (particularly to humans) include the time distribution of expression of the events, differences in experimental protocols, and variations among cell systems. (no Refs)

## 2. ULTRAVIOLET LIGHT SENSITIVITY AND PROLONGED UVR-ERYTHEMA.

**Wilson PD, Kaidbey KH, Kligman AM**
**(c/o Kaidbey), 3401 Market St., Suite 226, Philadelphia, PA, 19104**
**J Invest Dermatol; 77(6):434-436 1981**

We have compared the erythema and tanning responses in skin Type I (n = 15) and skin Type IV (N = 17) Caucasoids following a single exposure to solar simulated radiation. The former sunburn easily and do not tan while the latter do not burn and tan readily. The dose of radiation was 5x the Minimal Erythema Dose (MED). The test sites were the extensor aspect of the forearm (exposed site) and flexor aspect of the upper arm (nonexposed site). The responses were monitored at 24 and 48 hr and then twice weekly for 8 weeks. The group of skin Type I individuals had a lower MED and a much more prolonged erythema on both the exposed and nonexposed sites than the group of Type IV individuals. All differences were highly significant (p less than 0.005). After 4 weeks erythema remained present in all of the Type I subjects but had disappeared in 16 of the 17 Type IV subjects. Within the groups there was no difference between erythema duration on exposed vs nonexposed sites, but there was a highly significant difference (p less than 0.005) between the lower MED on the upper arm and higher MED on the forearm. These results contrast with those of other reports in which prolonged erythema could not be correlated with fair complexion, sunburn sensitivity, ethnic background, or skin type but was instead found to be a distinct feature of persons who had developed nonmelanoma skin cancer. Since prolonged erythema is related to skin type it is therefore not solely a feature of patients with skin cancer. (Author abstract) (10 Refs)

# EXPERIMENTAL RADIATION CARCINOGENESIS

## 3. RADIATION-INDUCED MAMMARY CARCINOGENESIS IN VIRGIN, PREGNANT, LACTATING, AND POS TLACTATING RATS.

**Holtzman S, Stone JP, Shellabarger CJ**
**Medical Dept., Brookhaven Natl. Lab., Upton, NY, 11973**
**Cancer Res; 42(1):50-53 1982**

Little attention has been paid to the influence of reproductive condition of the rat at the time of irradiation upon x-ray-induced mammary carcinogenesis. At 12 wk of age, 160 virgin female Sprague-Dawley rats were mated, and another 140 were maintained as virgins. On Days 14 to 16 of pregnancy, 36 mated females and 40 virgins were whole-body irradiated with 200 R of x-rays. On Days 2 to 5 postpartum, 40 additional mated females and 40 additional virgins were irradiated. At this time, all pups were removed from their mothers; 2 wk later, 40 additional parous females and 40 virgins were irradiated. The remaining animals: parous females; virgins; and mated, but nonparous females were kept as unirradiated controls. Brest tissue biopsies were taken from 25% of the animals in each irradiated group on the day of irradiation, and the biopsies were examined microscopically for mammary tissue development. The experiment was terminated 10 mo after irradiation. Despite marked differences in mammary tissue development among the groups at the time of irradiation, there were no significant differences among the irradiated groups for the incidence of rats with mammary adenocarcinomas or the number of mammary adenocarcinomas per rat. There were no significant differences among the irradiated groups for the incidence of rats with mammary fibroadenomas. There was an increase in the number of fibroadenomas per rat which was associated with increased age at the time of death. In contrast to mammary carcinogenesis produced by polycyclic aromatic hydrocarbons in previous studies, in the current investigation the physiological status of the host at the time of irradiation had little effect on: (a) the final incidence of mammary neoplasia; (b) the number of mammary adenocarcinomas produced; or (c) the type of mammary neoplasms produced. (Author abstract) (29 Refs)

## 4. EXPRESSION OF INITIATED AND PROMOTED STAGES OF IRRADIATION CARCINOGENESIS IN VITRO.

**DiPaolo JA, DeMarinis AJ, Evans CH, Doniger J**
**Lab. Biology, NCI, Bethesda, MD, 20205**
**Cancer Lett; 14(3):243-249 1981**

The temporal dynamics of 12-O-tetradecanoylphorbol-13-acetate (TPA)-promoted transformation in vitro and the sensitivity of initiation and promotion to lymphotoxin were investigated. Syrian hamster embryo cells (HEC) initiated by x-irradiation (300 R) were treated with TPA 48 hr later for transformation induction. TPA treatment resulted in a 15-20x enhancement of x-ray induced transformation. When cells were irradiated on day 1 and treated with TPA on days 3, 4, or 5 of the 7-day experiment, similar transformation frequencies resulted, indicating that TPA is required only for the last 2 days. All cells ap peared to be initiated on day 3. However, the presence of TPA from days 3-5 was found to be insufficient for max transformation. Since a return to levels of transformation obtained by x-irradiation alone occurs with decreasing intervals of TPA exposure, the promotion phenomenon is apparently reversible. Both TPA-dependent and TPA-independent initiation occurs after x-irradiation in this system. Lymphotoxin was found to inhibit TPA enhancement of UV or x-irradiation transformation of HEC. (15 Refs)

### 5. HYPERTHERMIC MODULATION OF X-RAY-INDUCED ONCOGENIC TRANSFORMATION IN C3H 10T1/2 CELLS.

**Clark EP, Hahn GM, Little JB**
**Dept. Radiation Medicine, Massachusetts General Hosp., Boston, MA, 02114**

**Radiat Res; 88(3):619-622 1981**

The effect of hyperthermia on the malignant transforming potential of x-rays was studied in the C3H mouse embryo cell line (10T1/2, clone 8). No transformed foci developed in nontreated cultures or in cultures exposed to hyperthermia alone. When hyperthermia was combined with x-rays, either a 43 C/60 min or a 45 C/15 min hyperthermic exposure preceding a 200-rad x-ray exposure, produced a 4-5-fold enhancement in mean transformation frequency as compared with that induced by x-rays alone. The yield of transformants for cells exposed to 200 rad following incubation at 43 C for 60 min was significantly higher than for those exposed to 200 rad alone (0.02 less than P less than 0.05). Heating times were important since shorter hyperthermic exposures did not result in transformation frequencies significantly higher than that induced by x-rays alone. A similar trend was also observed when transformation was scored on a per dish basis. The results suggested that the possibility of treatment-induced neoplasms should be considered before the design of combined hyperthermia-radiation treatment plans. (10 Refs)

### 6. HISTOGENESIS AND PROGRESSION OF ULTRAVIOLET LIGHT-INDUCED TUMORS IN HAIRLESS MICE.

**Kligman LH, Kligman AM**
**Univ. Pennsylvania, Medical Education Bldg./GM, Room 234, Philadelphia, PA, 19104**

**JNCI; 67(6):1289-1297 1981**

Tumor histogenesis and progression were studied in UV-irradiated albino (Skh:hairless-1) and lightly pigmented (Skh:hairless-2) hairless mice. A strongly carcinogenic dose of UV light was used, producing 100% tumor incidence by 35 wk. The light source emitted mainly UV radiation in the range of 280-320 nm and the less energetic UV radiation up to 400 nm. The resulting epidermal changes and neoplasms resembled those seen in the actinically damaged skin of humans. Microscopic lesions included benign hyperplasia, actinic keratoses, and squamous cell carcinoma in situ and with microinvasion. Clinical tumors were epithelial papillomas, fibropapillomas, keratoacanthomas, cystic keratomas, benign pigmented macules, cutaneous horn-like growths, exophytic and endophytic squamous cell carcinomas of several cytologic types, and fibrosarcomas. Even with this high high dose of UV radiation, not all of the small tumors progressed to cancer. Many regressed, including some keratoacanthomas, whereas others remained small and benign for the lifetime of the mouse. (Author abstract) (34 Refs)

## EXPERIMENTAL RADIATION MUTAGENESIS

### 7. MUTATION INDUCTION BY MONOCHROMATIC 254-NM AND 365-NM RADIATION IN STRAINS OF ESCHERICHIA COLI THAT DIFFER IN REPAIR CAPABILITY.

**Webb RB, Turner MA**
**Div. Biological and Medical Res., Argonne Natl. Lab., 9700 South Cass Ave., Argonne, IL, 60439**

**Mutat Res; 84(2):227-237 1981**

Tryptophan-independent revertants were induced by exposure to 254-and 365-nanometer monochromatic radiation in Escherichia coli strains WP2 (wild-type), WP2s (uvrA), WP6 (polA), and WP6s (polA uvrA) but not in WP5 (lexA), WP10 (reaA), or WP100 (recA uvrA). Data indicate that near-UV radiation produces mutations through the error-prone component of postreplicaton repair. Selective damage or inhibition to error-free and error-prone repair systems caused complete mutation responses at 365 nanometer. (35 Refs)

## EFFECTS OF IRRADIATION ON CHROMOSOMES AND DNA

### 8. DOUBLE-STRAND BREAKS IN DNA CAUSED BY REPAIR OF DAMAGE DUE TO ULTRAVIOLET LIGHT.

**Bradley MO**
**Merck Inst. for Therapeutic Res., West Point, PA, 19486**

**J Supramol Struct Cell Biochem; 16(4):337-343 1981**

Induction of double strand breaks (DSB) during repair of UV light (UVL) damage was studied in human cells. UV light at doses up to 300 joule (J)/square cm (cm2) did not directly induce detectable DNA DSB in normal (IMR-90) cells irradiated and held on ice until lysis. When IMR-90 cells were irradiated with 100-300 J/cm2 of UVL at room temperature and allowed to incubate in fresh medium at 37 C, a time and dose-related increase occurred in the rate of pH 9.6 elution and therefore number of DNA DSB. DSB began to appear 3 hr after UVL and continued to increase for 51 hr. Since the cells remain attached to the dishes up to 51 hr, and all the cells exclude trypan blue after 24 or 48 hr, the data suggest the DSB are not a secondary result of cell death. Using a neutral filter elution method for measuring small numbers of DSB, UVL was shown not to induce DSB in xeroderma pigmentosum (XP) complementation group A cells; the cells are unable to incise pyrimidine dimer and so cannot initiate excision repair; at the same time they are more sensitive to killing by UVL than normal cells. Thus, excision repair is implicated as a mechanism for DNA DSB formation after UVL. Repair-induced DSB may be potent lesions that lead to cytotoxicity, chromosomal aberrations, deletion mutations, and cellular transformation. (19 Refs)

### 9. EFFECT OF LOW DOSE RATE IONIZING RADIATION ON THE DIVISION POTENTIAL OF CELLS IN VITRO. VIII. CYTOGENETIC ANALYSIS OF HUMAN FIBROBLASTS.

**Bourgeois CA, Raynaud N, Dietloff-Zito C, Macieira-Coehlo A**
**Laboratoire de Pathologie Cellulaire, Institut des Cordeliers, 75005 Paris, France**
**Mech Ageing Dev; 17(3):225-235 1981**

Human embryonic and adult cells were irradiated with fractionated doses of low dose rate ionizing radiation starting early during their lifespan. Adult cells were found to be more sensitive than fetal cells to ionizing radiation in terms of the number of cells produced during the lifespan of the control and the irradiated cultures. Phase III adult control cells had fewer chromosomal aberrations than Phase-III embryonic control cells. After irradiation there was an increase in chromosomal aberrations in adult cells but no increase in embryonic cells beyond those found in the control cultures. It is suggested that cells that have a higher potential for chromosomal rearrangements survive better after low dose rate ionizing radiation. (Author abstract) (19 Refs)

### 10. THE INFLUENCE OF ANOXIA OR OXYGENATION ON THE INDUCTION OF CHROMOSOME ABERRATIONS IN HUMAN LYMPHOCYTES BY 15-MEV NEUTRONS.

**Prosser JS, Stimpson LD**
**Natl. Radiological Protection Board, Chilton, Didcot, Oxon OX11 ORQ, England**
**Mutat Res; 84(2):365-373 1981**

Human lymphocytes were analyzed for dicentric and total aberrations after 15 million electron volt megavoltage neutron irradiation given during anoxia or oxygenation. The oxygen-enhancement ratio ranged from 3.7 to 1.6. Oxygen evidently does not act as a dose-modifying agent in the system. Values for relative biologic effectiveness (RBE) were greatest at low neutron doses where the presence of oxygen did not affect the value obtained. At high doses, RBE values were greater for aberrations induced during anoxia. (30 Refs)

### 11. MUTAGENIC AND LETHAL EFFECTS OF [5-125I]IODO-2'-DEOXYURIDINE INCORPORATED INTO DNA OF MAMMALIAN CELLS, AND THEIR RBES.

**Miyazaki N, Fujiwara**
**(c/o Fujiwara) Dept. Radiation Biophysics, Kobe Univ. Sch. Medicine, Kusunoki-cho 7-5-1, Chuo-ku, Kobe 650, Japan**
**Radiat Res; 88(3):456-465 1981**

The mutagenic and lethal efficiencies of 125I decay, unifilarly incorporated as 5-iodo-2'-deoxyuridine (IdURD) into DNA [(125I)IdU/dT-DNA] of V79 Chinese hamster cells are described. The results are compared with those after exposure to the reference x-rays under frozen conditions, which minimize indirect and cellular metabolic effects such as DNA repair, age-response difference due to cycle traverse, and isotope dilution by cell division. The lethal and mutagenic effect of external x-rays in frozen state and at room temperature are compared. Unifilar IdU/dT cells were sensitized to x-ray killing 2x greater than at room temperature and 1.5x greater than at-79 C as normal (dT/dT) cells based on mean lethal dose. The rate of 6-thioguanine-resistance (6TGr) induction/rad was 6x greater than in IdU/dT cells than in the dT/dT cells after external x-irradiation at room temperature, and only 1.7x greater than at-79 C. Thus IdU/dT cells were more sensitized to x-ray killing and mutation. Indirect effects also played a role in these biological endpoints. The freezing effect on x-ray lethality was larger in IdU/dT cells than in dT/dT cells: mean lethal dose-reduction factors were 7.77 and 5.14, respectively. This difference suggests that x-ray-induced Auger phenomenon in iodine incorporated into DNA might enhance lethality in addition to a contribution of ordinal radicals. The efficiency and relative biological effectiveness (RBE) of cell inactivation and mutagenesis was examined. (34 Refs)

### 12. ULTRASONIC INDUCTION OF SISTER CHROMATID EXCHANGES IN HUMAN LYMPHOCYTES.

**Haupt M, Martin AO, Simpson JL, Iqbal MA, Elias S, Dyer A, Sabbagha RE**
**(c/o Martin) Dept. Obstetrics and Gynecology, Northwestern Univ. Medical, Chicago, IL**
**Hum Genet; 59(3):221-226 1981**

Sister chromatid exchange (SCE) frequencies were analyzed using 'real-time' ultrasound as an indicator of DNA damage induced in human lymphocytes. Studies showed consistent small effects of ultrasound on SCE frequencies. A range of exposure times and intensities was tested in a series of blind, randomized, in vitro experiments under spatial and sonographic conditions simulating exposure of a gravid abdomen and uterus. Minimizing the numbers and lengths of exposure per patient appears prudent. (30 Refs)

### 13. SPONTANEOUS AND INDUCED CHROMOSOME ABERRATIONS IN BONE MARROW OF MICE OF DIFFERENT STRAINS AND AGE.

**Lil'p IG, Korogodina IuV**
**Lab. Experimental Genetics, Inst. Medical Genetics, Moscow, USSR**
**Tsitologiia; 23(10):1174-1179 1981**

The frequency of spontaneous and radiation- or thiophosphamide induced chromosome aberrations was studied in the bone marrow of 2-and 10-17 mo old A/He, 101/H, CBA, C57BL/6, and BALB/c mice. The level of induced chromosome aberrations in C57BL/6 mice did not depend upon the age, while the mice of other strains showed age-dependent increase of the frequency of chromosome aberrations. (40 Refs) (In RUS)

### 14. POSTREPLICATIVE DNA REPAIR IN UV-IRRADIATED CHINESE HAMSTER CHO CELLS.

**Zhestianikov VD, Pinto RI, Tavartkiladze BA, Abramian DS**
**Inst. Cytology, Leningrad, USSR**
**Stud Biophys; 85(1):63-65 1981**

Postreplication DNA repair was studied in UV-sensitive and UV-resistant clones of chinese hamster CHO cells. The most UV-sensitive clone was found to have the most pronounced DNA damage and the least effective DNA repair. (3 Refs) (In RUS)

# OTHER CELLULAR EFFECTS OF IRRADIATION

## 15. IN VITRO CELLULAR REGULATION OF MONOCYTE FUNCTION: EVIDENCE FOR A RADIOSENSITIVE SUPPRESSOR.

**Kleinerman ES, Decker JM, Muchmore AV**
**Frederick Cancer Res. Center, Building 560, Room 21-77, Frederick, MD, 21701**
**J Reticuloendothel Soc; 30(5):373-379 1981**

Radiation was used in the following studies to better define and understand the interaction between human killer monocytes and their suppressor lymphocytes in a cytotoxic assay. Human mononuclear leukocytes become spontaneously cytotoxic to a variety of red blood cell targets after 7 days of in vitro culture. This phenomenon was independent of exogenous stimulus by Ag, Ab, or mitogen. Monocytes appeared to be the cytotoxic cell and were controlled by lymphocyte suppressor cells. In the present study, x-irradiation enhanced the magnitude of monocyte-mediated cytotoxicity generated and stimulated an earlier appearance of this cytotoxicity when compared with that of unirradiated mononuclear leukocytes. The effect of x-irradiation (150 to 600 R) on separated populations of mononuclear leukocytes enriched for either lymphocytes or monocytes was examined; this enhanced cytotoxicity appeared to be secondary to inactivation of the lymphocyte suppressor cells. (Author abstract) (11 Refs)

# THEORETICAL ASPECTS OF RADIATION CARCINOGENESIS

## 16. IS ‘NO-THRESHOLD’ A ‘NON-CONCEPT’?

**Schaeffer DJ**
**Illinois Environmental Protection Agency, 2200 Churchill Road, Springfield, IL, 62076**
**Environ Manage; 5(6):475-481 1981**

The existence of a threshold for induction of cancer by an environmental agent is discussed. The induction of cancer is caused by chemicals or radiation which supply the energy to alter specific biochemical pathways. This process is governed by the laws of thermodynamics; thus the probability that a single molecule will cause any effect, even in a single cell, is zero. Dose response curves, which estimate the amount of the chemical that reacts with a selected target molecule, provide biologically significant estimates of threshold. Exposure response curves, however, reflect the majority of available data and permit the expression of health protection criteria in the terms of ordinary human activity. The carcinogenic threshold level can theoretically be estimated as 10,000 inducing events (carcinogen molecules) per cell. The management significance of non zero threshold is that the zero risk departure point for risk assessment is now the natural background level rather than an absolute zero level of exposure. (23 Refs)

## 17. THRESHOLD EXAMINATION FROM THE LINEAR DOSE-RESPONSE MODEL: METHOD AND RADIATION DATA.

**Schaeffer DJ, Janardan KG, Kerster HW**
**Div. Water Pollution, Illinois Environmental Protection Agency, 2200 Churchill Road, Springfield, IL, 62706**
**Environ Manage; 5(6):515-520 1981**

Predicting a carcinogenic threshold level by means of the linear dose response model is presented. Linear regression is most often used to extrapolate experimental data to lower doses; ability to estimate the threshold itself has not been established. Defining the threshold as the lowest dose with a response distinguishable from background may force technology to develop more precise and rapid techniques and may help restore credibility to the regulatory process. (19 Refs)

## 18. THE ATOMIC BOMB SURVIVORS AND THE PROBLEM OF LOW-DOSE RADIATION EFFECTS.

**Beebe GW**
**Clinical Epidemiology Branch, NCI-NIH, Room 5A21 Landow Building, Bethesda, MD, 20205**
**Am J Epidemiol; 114(6):761-783 1981**

The effects of low-dose radiation (0.1 to several rads/yr continuously or up to 10-20 rads in a single dose) are discussed in relation to data accumulated on atomic bomb survivors (ABS). Although ABS provide the largest available resource for human studies on the genetic effects of ionizing radiation, their number is not large enough to give direct information on effects in the low-dose region; a dose-response relationship does seem to exist for both Hiroshima and Nagasaki ABS. The relationship between radiation and disturbances in growth and development, somatic cell chromosomal aberrations, and carcinogenesis are discussed. Dose-response models are considered in relation to leukemia in ABS. Even with 550 cases observed in ABS between 1946 and 1974, determination of the real low-dose risk has not been possible. Using ABS data, a linear model appears suitable for the description of breast cancer incidence following low-dose radiation. Data from ABS survivors provide little information on the incidence of thyroid cancer following low-dose radiation from ABS. The relationship between low-dose, low linear energy transfer and other cancers observed in ABS is discussed. (60 Refs)

## 19. EPIDEMIOLOGY OF BREAST CANCER. PREVENTIVE ASPECTS.

**Modan B**
**Dept. Clinical Epidemiology, Chaim Sheba Medical Center, 52103 Tel-Hashomer, Israel**
**Isr J Med Sci; 17(9/10):804-809 1981**

Descriptive data demonstrate a marked variation in the incidence of breast cancer in distinct populations, which is closely linked to socioeconomic status and correlated with a differential age-specific incidence pattern and time trends. These suggest a westernization effect, and the possible existence of two distinct disease entities - pre- and postmenopausal. Known risk factors may be defined in a number of ways. From a preventive standpoint, a practical classification is suggested whereby risk factors are grouped as preventable, modifiable, unapproachable or spurious. The only risk factors which seem definite at present are estrogen exposure, family history and radiation, with the possible contribution of benign breast disease, replacement hormones, and diet. The only preventable factors are radiation and possibly long-term hormonal replacement, but their contribution to the disease incidence in the population is minimal. Two theoretically modifiable factors are diet and age at first birth, but the latter cannot be easily influenced, and the effect of dietary modification is still unsubstantiated. (Author abstract) (45 Refs)

### 20. LOW-DOSE RADIATION. RISKS VS BENEFITS.

**Upton AC**
**Inst. Environmental Medicine, New York Univ. Medical Center, 550 First Ave., New York, NY, 10016**
**Postgrad Med; 70(6):34-37,40-41,45-47 1981**

Low-level ionizing radiation may have carcinogenic, mutagenic, or teratogenic effects. The risks of carcinogenic effects in exposed individuals are thought to compare in magnitude with the risks of genetic effects in their descendants. With abandonment of the threshold hypothesis for radiation mutagenesis and carcinogenesis, any exposure to radiation must be assumed to carry some risk. The risk-benefit trade-off is likely to be socially unacceptable unless the expected benefits greatly outweigh the presumed risks. (Author abstract) (17 Refs)

## ENVIRONMENTAL RADIATION AND PROTECTION STANDARDS

### 21. RADIOBIOLOGICAL INPUT TO RADIATION PROTECTION STANDARDS.

**Bond VP**
**Brookhaven Natl. Lab., Upton, NY, 11973**
**Health Phys; 41(6):799-806 1981**

A survey of the radiobiological literature was undertaken by Committee 40 of the National Council on Radiation Protection. Whether the 'linear-no threshold' hypothesis of the genetic effects of radiation pertains to carcinogenesis and whether a 'dose rate factor' (as assumed for mutagenesis) exists for human carcinogenesis was examined. The general nature of the findings is illustrated by data on pink mutations induced in Tradescantia by x-rays, gamma-radiation, and linear energy transfer radiation. Exposure-response curves for all the radiation types were linear at low doses but had different slopes depending on the quality of radiation. Overall incidence-dose curves appeared to be the sum of two radiation components, one capable of single-hit kinetics and the other capable only of multi-hit kinetics. Relationships developed in the Tradescantia system should hold true for both mutagenesis and human carcinogenesis. A risk coefficient of 1 x 10(-4)/roentgen-equivalent-man is most suitable for the weighted risk of radiation-induced cancers and mutations. (18 Refs)

### 22. MAMMOGRAPHY - MISUNDERSTOOD AND UNDERUTILIZED.

**Broadbent RV, Reid MH**
**Veterans Admin. Hosp., 1000 Locust Dr., Reno, NV, 89520**
**Postgrad Med; 70(6):93-97,100-101 1981**

A mammography screening program for breast cancer carried out in Sacramento by the University of California Davis School of Medicine, Davis, was canceled because of negative public reaction to sensationalized reports in the lay press on the potential carcinogenic risks of the radiation exposure, along with passivity on the part of the medical community in defending the procedure and the program. Disappointment in this occurrence spurred us to explore physicians' knowledge of and attitudes toward breast cancer and mammography. The results confirmed our suspicions that a significant number of physicians lack accurate knowledge of breast cancer and of the extremely high benefit-to-risk ratio of mammography as a means of early detection. (Author abstract) (8 Refs)

### 23. CARCINOGENIC RISK OF EXPOSURE TO RADON DAUGHTERS ASSOCIATED WITH RADON SPAS.

**Uzunov I, Steinhausler F, Pohl E**
**Faculty Physics, Univ. Sofia, BG-1126 Sofia, Bulgaria**
**Health Phys; 41(6):807-813 1981**

Water, containing high concentration of 222Rn naturally or artificially, is used worldwide for therapeutical treatment of different diseases. In some radon spas people use the mineral water source without any limitation. High concentration of radon and its short-lived decay products has been measured indoors in radon treatment centers and even private houses. No recommendations from international organizations deal with the potential risk for the patients and only a few countries apply radiation protection measures for the personnel. The radioactive environment of two different radon spas is described. It is demonstrated that in both cases not only the patients, but also the staff, and even the general public of such a spa (including children and youths) are exposed to increased dose levels, mainly due to inhalation of radon decay products. Carcinogenic risks are assessed, taking into consideration age dependence of dose and risk. Risk data was derived from epidemiological studies of uranium miners, since no such data are available for inhabitants of radon spas. The results show that in some cases the risk is unacceptably high. The calculations presented can be also useful for the assessment of risk in other environments, such as in dwellings with increased content of atmospheric randon daughters, eg due to the building material used. (Author abstract) (37 Refs)

### 24. SOMATIC RADIATION RISK IN VARIOUS MAMMOGRAPHY TECHNIQUES.

**Ewen K, John V, Von dem Driesch P**
**Zentralstelle fur Sicherheitstechnik des Landes Nordrhein-Westfalen, Gurlittstr. 53a, 4000 Dusseldorf, W. Germany**
**Roentgenpraxis; 34(12):488-492 1981**

Somatic radiation risks (SRR) were calculated for mammography techniques, including mammography/x-ray-enrichment using Senographe 1, Senographe 500T, and Mammodiagnost U systems, xerographic enrichment using the Type S 125 Xerox system, and the Mammography Detail Phantom system. SRR increased in proportion to increasing image quality. Selection of technique therefore requires careful balancing of risk against benefit in individual cases. (9 Refs) (In GER)

## REVIEWS AND OTHER STUDIES

### 25. DOSIMETRY OF THE ATOMIC BOMB SURVIVORS.

**Sinclair WK, Failla P, Bond VP, Loewe WE, Kerr GD, Auxier J, Wyckoff OH, Maruyama T, Schull JW, Land EC, Dobson LR, Mays WC, Seymour J**
**Argonne Natl. Lab., 9700 South Cass Ave., Argonne, IL, 60439**
**Radiat Res; 88(3):437-447 1981**

A summary of information presented at the Late Effects Workshop on Dosimetry of the Atomic Bomb Survivors was compiled. The relevance of findings obtained on Japanese atomic bomb survivors for the determination of radiation risk estimates is discussed through a review of the history, status and implications of the dosimetry of the survivors. In a study of the radiobiological significance of the HIroshima/Nagasaki data, it was determined that there are qualitative differences between the two cities which suggest the presence of a high-linear energy transfer component at Hiroshima. These include the shapes of the curves for chromosomal aberrations and a difference in the spectrum of leukemia types in the two cities. In another presentation, it was suggested that for Hiroshima, at 2 kilometers, the T65 neutron doses were 9x too high, and the gamma doses 4x too low; the uncertainties (approx a factor of 2) in these estimates can be reduced by additional effort. Another presentation reviewed problems associated with calculating dosimetry for the Japanese atomic bomb survivors. The Ichiban studies showed that the sulfur-activation data from Hiroshima and Nagasaki were in reasonable agreement with T65 doses. The difficulty in correlating the chromosome aberration results found in the two cities with the doses predicted by new calculations is considered. The role of the National Council on Radiation Protection and Measurements in Hiroshima and Nagasaki dosimetry is discussed. Primary points brought out in discussions associated with the symposium are listed. (7 Refs)

### 26. GENETIC AND BIOCHEMICAL STUDIES WITH ATAXIA TELANGIECTASIA.

**Huang PC, Sheridan RB**
**Dept. Biochemistry, Sch. Hygiene and Public Health, Johns Hopkins Univ., Baltimore, MD, 21205**
**Hum Genet; 59(1):1-9 1981**

Correlation of the clinical symptomatology with the genetics and biochemical studies of cultured cells derived from patients with ataxia telangiectasia (AT) is presented in a review. The genetics and symptomatology of AT are described. The susceptibility of patients with AT to sino-pulmonary infection and predisposition toward lymphoreticular malignancy may be caused by immunodeficiency involving humoral and/or the cellular immune system. Approx 10% of patients with AT develop cancer. Response of AT patients to radiation is discussed. Recent cytogenetic, cellular, and biochemical studies are reviewed which support the hypothesis that a defect in DNA repair is responsible for the many manifestations of AT. A table summarizes biochemical studies of 25 factors in 19 cell lines, all but four of which were d erived from AT homozygotes. The biochemical evidence indicates that the defect specifically reduces the cellular capacity to remove bases and nucleotides damaged by ionizing radiation, without affecting the cells' ability to scavenge free radicals or to rejoin breaks in the sugar-phosphate backbone of DNA. (72 Refs)

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# NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

## CHEMICAL CARCINOGENESIS

1. CHEMICAL CARCINOGENESIS.
Farber E
Dept. Pathology, Univ. Toronto, 100 College St., Toronto, ON M5G 1L5, Canada
N Engl J Med; 305(23):1379-1389 1981

2. N-HEXANE AND ITS TOXICOLOGIC EFFECTS. A REVIEW.
Jorgensen NK, Cohr KH
Harevaenget 44, DK-4200 Slagelse, Denmark
Scand J Work Environ Health; 7(3):157-168 1981

3. SAFROLE: ITS METABOLISM CARCINOGENICITY AND INTERACTIONS WITH CYTOCHROME P-450.
Ioannides C, Delaforge M, Parke DV
Dept. Biochemistry, Univ. Surrey, Guildford, Surrey GU2 5XH, England
Food Cosmet Toxicol; 19(5):657-666 1981

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Suit H, Hall E, Frei E
Dept. Radiation Medicine, Massachusetts General Hosp., Boston, MA, 02114
Cancer Clin Trials; 4(Suppl):37-41 1981

5. DOSIMETRY OF THE ATOMIC BOMB SURVIVORS.
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Argonne Natl. Lab., 9700 South Cass Ave., Argonne, IL, 60439
Radiat Res; 88(3):437-447 1981

## DIETARY FACTORS IN CARCINOGENESIS

6. NUTRITION AND CANCER: A REVIEW.
Muller E, Rickenbach M
Institut fur Sozial- und Praventivmedizin, Universitat Zurich, Gloriastrasse 32 B, 8006 Zurich, Switzerland
Praxis; 70(43):1903-1912 1981
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U. S. Dept. Agriculture, Agricultural Res. Service, Fruit and Vegetable Chemistry Lab., Pasadena, CA, 91106
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## EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

8. ETIOLOGICAL CONCEPTS IN CERVICAL CARCINOGENESIS.
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Dept. Epidemiology and Preventive Medicine, Univ. Maryland Sch. Medicine, 655 West Baltimore St., Baltimore, MD, 21201
Gynecol Oncol; 12(2,part2):S7-S24 1981

9. CURRENT CONCEPTS ON THE AETIO-PATHOGENESIS OF ACUTE LEUKAEMIA.
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Jefe Servicio Hematologia, Ciudad Sanitaria 'Reina Sofia' de la Seguridad Social, Cordoba, Spain
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Kirurgisk-gastroenterologisk afdeling, Bispebjerg hospital, Copenhagen, Denmark
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12. THE HEALTH EFFECTS AND ECOLOGICAL SIGNIFICANCE OF CHLORINE RESIDUALS IN WATER.
Kalmaz EV, Kalmaz GD
Univ. Tennessee, Univ. Station 8163, Knoxville, TN, 37916
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14. THE REPAIR OF DNA DAMAGE: RECENT DEVELOPMENTS AND NEW INSIGHTS.
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Dept. Pathology, Lab. Experimental Oncology, Stanford Univ., Stanford, CA, 94305
J Supramol Struct Cell Biochem; 16(1):91-103 1981

## MODIFICATION OF CARCINOGENESIS

15. ROLE OF HORMONES INCLUDING DIETHYLSTILBESTROL (DES) IN THE PATHOGENESIS OF CERVICAL AND VAGINAL INTRAEPITHELIAL NEOPLASIA.
Robboy SJ, Truslow GY, Anton J, Richart RM
Dept. Pathology, Massachusetts General Hosp., Boston, MA, 02114
Gynecol Oncol; 12(2,part2):S98-S110 1981

16. PROSTAGLANDINS AND CANCER: A REVIEW OF TUMOR INITIATION THROUGH TUMOR METASTASIS.
Honn KV, Bockman RS, Marnett LJ
Dept. Biological Sciences, Wayne State Univ., Detroit, MI, 48202
Prostaglandins; 21(5):833-864 1981

## VIRAL AND IMMUNOLOGICAL ASPECTS OF CARCINOGENESIS

17. GENITAL CANCER AND VIRUSES.
Rapp F, Jenkins FJ
Dept. Microbiology, Pennsylvania State Univ. Coll. Medicine, Hershey, PA, 17033
Gynecol Oncol; 12(2,part2):S25-S41 1981

18. VIRUS PAPILLOMAS IN HUMANS.
Nasemann T
Univ.-Hautklinik Eppendorf, Martinistr. 52, D-2000 Hamburg 20, W. Germany
Hautarzt; 32(11):601-606 1981
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## RADIATION CARCINOGENESIS IN HUMANS

### 1. CANCER EPIDEMIOLOGY.

**Sancho-Garnier H, Flamant R**
**Departement de Statistique Medicale et Unite de Recherches Statistiques, 94800 Villlejuif, France**
**Rev Infirm; 31(17):19-27 1981**

Standardized cancer mortality rates for 1973 yr set France in third place, behind West Germany, England, and Wales. In France, the overall cancer mortality was 221 per 100,000 inhabitants but men were affected twice as often as women. The increase of cancer mortality rate from 1954-1976 was attributed to the increase in cancer deaths among men due to lung cancer

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and cancers of the upper gastrointestinal and pulmonary tracts. Deaths from cancer represented about 20% of general mortality and a third of the deaths for men in the 55-75 yr range and for women in the 35-55 yr range. Analytical epidemiology has determined the probable causative factors of various types of cancers. These etiological agents include tobacco, pollution, ultraviolet or ionizing radiation, alcohol, nutrition, hormones, infections, immunology, and genetic factors. Cancer has also been linked to certain immunosuppressive and cytotoxic drugs. Resistance to epidemiological data is steadfast not only because pleasurable pursuits such as drinking and smoking are involved but also because the economic consequences of change are staggering. However, more than half of the cancer cases would be affected by alcohol and tobacco campaigns and by the early screening and treatment of cancers of the breast and uterus. (17 Refs) (In FRE)

### 2. IRRADIATION-RELATED THYROID CANCER: INFLUENCING THE HEALTH BEHAVIOR OF HIGH RISK INDIVIDUALS THROUGH MASS MEDIA AND A TELEPHONE INFORMATION SERVICE (MEETING ABSTRACT).

**Stein JA**

**Division of Resources, Centers and Community Activities, National Cancer Institute, Bethesda, MD**

**Proceedings of the 15th Annual Meeting of the American Association for Cancer Education, November 11-14, 1981, San Diego, California. The Association 73 pp., 1981.**

A study was performed to determine the factors influencing the health behavior of individuals at risk for irradiation-related thyroid cancer. Estimates of the number of persons who have received these treatment ranges from hundreds of thousands to over a million. However, patient recall programs carried out by hospitals and physicians have encountered difficulty in locating patients whose names had changed or who had relocated in the many years subsequent to treatment. In addition, this type of follow-up is expensive and time consuming. Therefore, a public education approach was recommended by the (NCI) to reach this population. The media learned of this problem in 1977 during the first NCI 'media alert' for an at-risk population. Although the problems gained media attention, there was no way to measure its impact on the health behavior of the target population. Its impact on a Cancer Information Service (CIS) office, a telephone information system funded by NCI, was significant. Whenever the media featured the problem of irradiation-related thyroid cancer, hundreds of calls were received on the topic. In order to survey the health behavior of this high risk group, an article was placed in a large metropolitan newspaper. The telephone number of the CIS office was given as a resource for further information and suggestions for follow-up. One hundred and thirty-one individuals who called the CIS after reading this article were surveyed regarding their health behavior following contact with a CIS telephone counselor. Seventy-seven responses were received from individuals who were members of the population at risk. The results of the survey indicated that although 79% were already aware of their 'at-risk' status prior to contact with the CIS, only two had sought medical attention. However, following the person-to-person contact over the telephone with a CIS staff member, all but four callers were persuaded to seek medical attention. (no Refs)

### 3. NEOPLASMS FOLLOWING CHILDHOOD RADIUM IRRADIATION OF THE NASOPHARYNX.

**Sandler DP, Comstock GW, Matanoski GM**

**Biometry Branch, Epidemiology Program, Natl. Inst. Environmental Health Sciences, P.O. Box 12233, Research Triangle Park, NC, 27709**

**JNCI; 68(1):3-8 1982**

Eighteen to 35 years after admission to a clinic for the prevention of deafness, no increased overall cancer risk could be detected among 904 persons who had been treated with nasopharyngeal radium irradiation when compared with the risk among 2,021 persons who were either treated surgically or not treated at all, although there were differences at specific sites. An increased risk of developing both benign and malignant head and neck tumors was found among irradiated persons. Whereas no one head and neck site showed a statistically significant excess, a slight excess of brain cancer occurred 15-20 years after radium treatment. No increase in thyroid cancer risk was observed, a result possibly attributable to the low radiation doses to this organ and the relatively small population irradiated. (Author abstract) (27 Refs)

### 4. A STUDY OF THE MORTALITY OF CORNISH TIN MINERS.

**Fox AJ, Goldblatt P, Kinlen LJ**

**Medical Statistics Div., Office of Population Censuses and Surveys, London, England**

**Br J Ind Med; 38(4):378-380 1981**

Increased mortality from cancer of the lung has been found in several studies of miners exposed to high levels of radioactivity in underground air. In view of their exposure to raised levels of radiation, we have studied the mortality of a group of men recorded as Cornish tin miners in 1939. Using occupational description, a crude classification of exposure was derived for these miners. The meaningfulness of this classification was supported by differences in mortality for silicosis and silicotuberculosis. A twofold excess of cancer of the lung was found from underground miners, while for other categories mortality from this cause was less than expected. This supports the findings of previous studies on exposure to radon and its daughters. An excess of cancer of the stomach was also observed among underground miners. (Author abstract) (15 Refs)

## EXPERIMENTAL RADIATION CARCINOGENESIS

### 5. ANTIPAIN AND RADIATION EFFECTS ON ONCOGENIC TRANSFORMATION AND SISTER CHROMATID EXCHANGES IN SYRIAN HAMSTER EMBRYO AND MOUSE C3H/10T1/2 CELLS.

**Geard CR, Rutledge-Freeman M, Miller RC, Borek C**

**Radiological Res. Lab., Dept. Radiology, Columbia Univ. Coll. Physicians and Surgeons, New York, NY, 10032**

**Carcinogenesis; 2(12):1229-1233 1981**

Depending on its time of addition to Syrian hamster embryo or mouse C3H 10T1/2 cells the protease inhibitor antipain (AP) can enhance, or reduce, radiation induced-oncogenic transformations. These opposing influences are not paralleled by changes in sister chromatid exchanges in either cell system. A 24 hr treatment with 10 uM AP prior to, and during irradiation, with removal 10 min after irradiation results in greater than a two-fold increase in transformants. Conversely, a 24 hr treatment beginning 10 min after irradiation results in about a two-fold decrease in transformants. The utility of AP as an agent for the reduction of tumorigenesis is brought into question, since quite short temporal differences in application can result in near five-fold differences in the frequencies of oncogenic transformations. (Author abstract) (32 Refs)

### 6. ENHANCED TRANSFORMATION OF MOUSE 10T1/2 CELLS BY 12-O-TETRADECANOYLPHORBOL-13-ACETATE FOLLOWING EXPOSURE TO X-RAYS OR TO FISSION-SPECTRUM NEUTRONS.

**Han A, Elkind MM**
**Mammalian Cell Biology Group, Div. Biological and Medical Res., Argonne Natl. Lab., Argonne, IL, 60439**
**Cancer Res; 42(2):477-483 1982**

Addition of the tumor promoter 12-O-tetradecanoylphorbol-13-acetate (TPA) to C3H/10T1/2 cells after exposure to either x-rays or to fission-spectrum neutrons increases significantly the frequency of transformation without any effect on cell survival. However, treatment of unirradiated cells with 0.1 ug of TPA per ml alone results in a small increase in transformation frequency above background (ie, from 1.1 x 10(-5) to 1.0 x 10(-4)). Thus, besides being a promoter, TPA is also a weak initiator. Enhancement of radiation-induced transformation by TPA was relatively greater after low compared to high doses of either radiation. In addition, TPA causes the relative biological effectiveness of neutrons compared to x-rays to increase with increasing dose or with increasing frequency of transformation rather than to decrease, when TPA is not used. For x-ray doses from zero to approx 120 rads, TPA raises transformation to frequencies approx equal to those due to neutrons alone. Analysis of TPA enhancement in the context of the combined effect of two inducing agents, ie, TPA plus a radiation, indicates that with either radiation TPA acts synergistically. Lastly, TPA was found to alter the dependence of transformation frequency on the density of viable cells. As opposed to a constant frequency of transformants per surviving (or viable) cell, which we observed after a fixed dose of x-rays or neutrons for a range of cell inocula the addition of TPA increased the frequency of transformation for all cell inocula (ie, from approx 20 to 6,000 viable cells per 90-mm Petri dish). However, the frequency of transformation decreases with increasing size of the inoculum, a result that we interpret to indicate the combined effect of an interference with cell-to-cell communication by TPA plus the fading of initiation events due to the radiation. (Author abstract) (41 Refs)

### 7. EQUIVALENCY OF ENDOTHELIAL CELL GROWTH SUPPLEMENT TO IRRADIATED FEEDER CELLS IN CARCINOGEN-INDUCED MORPHOLOGIC TRANSFORMATION OF SYRIAN HAMSTER EMBRYO CELLS.

**Evans CH, DiPaolo JA**
**Lab. Biology, Div. Cancer Cause and Prevention, NCI, Bethesda, MD, 20205**
**JNCI; 68(1):127-131 1982**

Endothelial cell growth supplement (ECGS), an extract of bovine neural tissue with growth-promoting properties for human endothelial and epithelial cells and for mouse BALB/c fibroblast-like cells, can be substituted for feeder cells in a quantitative 7-day Syrian hamster embryo cell colony in vitro model of carcinogenesis. Inclusion of 50 or 100 ug ECGS/ml medium throughout the 7-day growth period produced results equal to those obtained with feeder cells. The frequency and morphology of normal fibroblast colonies and carcinogen-induced morphologically transformed cell colony growth in the presence of ECGS were similar to those in the presence of feeder cells. A positive dose-response relationship in transformation by benzo[a]pyrene occurred. The frequency of transformed colonies following UV irradiation and treatment of the cells with the cocarcinogenic tumor promoter 12-O-tetradecanoylphorbol 13-acetate was greatly augmented, and lymphotoxin, a lymphokine with anticarcinogenic activity, reduced transformation. Thus ECGS can substitute for feeder cells in supporting in vitro transformation and eliminates a potential complex source of variability for studies where interaction(s) with feeder cells are a consideration. The mechanics of this model system was simplified, and its versatility for the study of physiologic, carcinogenic, and other pathophysiologic processes was broadened. (Author abstract) (19 Refs)

### 8. EFFECT OF AN ESTROGEN ANTAGONIST (TAMOXIFEN) ON THE INITIATION AND PROGRESSION OF GAMMA-IRRADIATION-INDUCED MAMMARY TUMORS IN FEMALE SPRAGUE-DAWLEY RATS.

**Welsch CW, Goodrich-Smith M, Brown CK, Miglorie N, Clifton KH**
**Dept. Anatomy, Michigan State Univ., East Lansing, MI, 48824**
**Eur J Cancer Clin Oncol; 17(12):1255-1258 1981**

One hundred and sixty-eight female Sprague-Dawley rats were divided among four groups (42 rats/group) and were irradiated with 400 rad [137Cs] gamma rays to the whole body when 59 days old. The estrogen antagonist tamoxifen was injected sc daily from 29-89 days of age (Series 1) or from 89-149 days of age (Series 2), prior to the onset of palpable mammary tumors. Two groups of rats were injected with the diluent and served as controls. All rats were palpated bi-weekly for mammary tumors and killed 37 wk after gamma-irradiation. The number of mammary carcinomas which developed in each group and their significance levels were: series 1, controls, 31; tamoxifen treated, 11, p less than 0.01; series 2, controls, 33; tamoxifen treated, 17, p less than 0.01. Tamoxifen treatment did not significantly influence the incidence of benign mammary tumors (fibroadenomas) nor the rate of body wt gain. Thus, the effective use of an estrogen antagonist for the prophylaxis of radiogenic mammary carcinomas has been demonstrated in this study. (Author abstract) (13 Refs)

### 9. THE EPIDEMIOLOGY OF SQUAMOUS CELL CARCINOMA OF THE PERINEAL REGION OF SHEEP.

**Hawkins CD, Swan RA, Chapman HM**
**Sch. Veterinary Studies, Murdoch Univ., Perth, Western Australia 6150, Australia**
**Aust Vet J; 57(10):455-457 1981**

A postal survey concerning pasture and livestock management practices that could contribute to the epidemiology of squamous cell carcinoma of the perineal region of ewes was conducted in areas of Western Australia where the disease was reported on 64 of 78 farms (82%). Prevalence on affected farms ranged from 0.12% to 4.0% (av 2.29%). Prevalence was low (0.5%) in 1-2-yr-old ewes, and increased with age and was 3.09% in ewes greater than 5 yr old. The vulva, tail, and perineum were affected in 88.9%, 23.8%, and 12.8% of cases, respectively. The sheep were predominantly Merino, mostly of the Collinsville strain. On a significantly higher proportion of affected than unaffected farms, ewes were shorn between January and June; times of shearing other mobs of sheep (ie, lambs, rams, and wether) were not different between affected and unaffected farms. Mulesing and tail docking procedures and the proportion of farms serviced by different mulesing contractors were similar for affected and unaffected farms. 'Skin cancer' at sites other than the perineum (nose, ears, face) occurred in 22% of the affected flocks, versus 14% of unaffected flocks. Possible roles of shearing time and solar radiation in the development of perineal cancer of sheep should be investigated. In addition, possible interactions of these factors with the Mules operation and tail length need to be studied further, as the sites of squamous cell carcinoma of the perineum of ewes almost invariably include areas exposed by the radical Mules operation. (8 Refs)

### 10. ENDOGENOUS MULV INFECTION DOES NOT CONTRIBUTE TO ONSET OF RADIATION- OR CARCINOGEN-INDUCED MURINE THYMOMA.

**Mayer A, Dorsch-Hasler K**
**Dept. Pathology, New York Univ. Sch. Medicine, 550 First Ave., New York, NY, 10016**
**Nature; 295(5846):253-255 1982**

The contribution of endogenous murine leukemia virus (MuLV) to onset of radiation- or carcinogen-induced murine thymoma was examined. The effect of cellular Fv-1 locus on the development of radiation-induced thymic lymphoma was tested to determine whether this form of induced thymoma also requires active MuLV infection. RF/J and BALB/cJ strains of mice were highly susceptible to radiation induction of thymoma. To measure the effect of Fv-1 more directly, the incidence of radiation-induced thymoma was determined in (BALB/c x RF)F1 x RF backcross mice typed for the alleles carried at the Fv-1 locus. Fv-1n homozygous and Fv-1n/Fv-1b heterozygous backcross mice were identified by typing each backcross mouse for its phenotype at the Gpd-1 locus, which is closely linked to the Fv-1 locus. The two subpopulations of the backcross did not differ substantially in radiation-induced thymoma incidences. The finding are not consistent with a requirement for active infection by endogenous MuLV in the development of radiation-induced thymoma. When the backcross mice were typed for their haplotype at H-2, no H-2-associated effect was observed to influence relative resistance to radiation-induced thymoma. RF and 129 mice were chosen for induction of thymoma by N-nitrosomethylurea. Both strains showed high sensitivity. RF mice are much more sensitive to radiation-induced thymoma than 129 mice. F1 hybrid mice also developed a high incidence of the tumor. These findings indicate a basic difference between the etiologies of spontaneous and carcinogen- or radiation-induced thymoma. Spontaneous occurrence of the tumor is associated with expression of endogenous mouse-infectious MuLV activities, including both XC-positive and XC-negative ecotropic MuLV and dualtropic MCF MuLV. Active infection of cells by endogenous MuLV is not essential to development of thymic lymphoma in the mouse following exposure to radiation or chemical carcinogens. (23 Refs)

### 11. PULMONARY TUMOURS IN SYRIAN HAMSTERS FOLLOWING INHALATION OF 239PUO2.

**Thomas RG, Drake GA, London JE, Anderson EC, Prine JR, Smith DM**
**Life Sciences and Health Div., Los Alamos Natl. Lab., Univ. California, Los Alamos, NM, 87545**
**Int J Radiat Biol; 40(6):605-611 1981**

Syrian hamsters were exposed to various levels of aerosolized 239PuO2 particles to attain a range of initial lung burdens (medians ranged from 40 to 144nCi). They were allowed to live without sacrifice and had gross and microscopic tissue examinations at death. Over a range of median lung doses from 4-12,000 rad there was an av 2% incidence of malignant tumors (adenocarcinomas) and 9% incidence of total tumors (primarily adenomas). Some of these results are consistent with those from other laboratories using plutonium oxide aerosols but they represent considerably lower lung tumor incidences than previously observed in this laboratory using aerosols of 238PuO2-ZrO2 particles. (Author abstract) (13 Refs)

## EXPERIMENTAL RADIATION MUTAGENESIS

### 12. ANTIMUTAGENIC ACTIVITIES OF HUMAN PLACENTAL EXTRACT ON ULTRAVIOLET LIGHT- AND GAMMA-RAY-INDUCED MUTATION IN ESCHERICHIA COLI WP 2 B/R TRP.

**Kada T, Mochizuki H**
**Dept. Induced Mutation, National Inst. Genetics, Mishima, Shizuoka-ken 411, Japan**
**J Radiat Res (Tokyo); 22(3):297-302 1981**

Antimutagenic activities of human cells on radiation-induced cellular mutagenesis were studied. The Escherichia coli strain WP2 B/r trp was used. A germicidal lamp was used for UV irradiation of a cold suspension of bacteria in phosphate buffer solution. Gamma-ray irradiation with a 137Cs source at a dose rate of 33 kilorad/hr was performed on bacterial cells kept in ice-water. Experiments were performed to confirm that the reduction of induced trp positive (Trp+) colonies results from antimutagenic effects during radiation-induced mutagenesis. The sensitivity of Trp+ clones to human placental extract was studied under conditions comparable to those of the antimutagenicity assay. Results showed that the number of induced mutant colonies decreased significantly with UV- and gamma-irradiation; effects of placental extract on the survival of Trp+ colonies were not as significant. The extract is not mutagenic, and results indicate that it contains factors which antagonize UV- or gamma-ray-induced mutations in bacteria. Results of reconstruction experiments show that the Trp+ cells are not particularly sensitive to the placental extract on UV- or gamma-ray induction. Human placental extract apparently works not on the expressed Trp+ mutant cells but rather in the course of mutagenesis. Presence of the antimutagenic factor in human placental tissues is of interest if it indeed reduces radiation-induced mutations in the embryo. (8 Refs)

## EFFECTS OF IRRADIATION ON CHROMOSOMES AND DNA

### 13. X-RAY INDUCED CHROMOSOME ABERRATIONS IN DOWN LYMPHOCYTES: AN EXPLANATION OF THEIR INCREASED SENSITIVITY.

**Preston RJ**
**Biology Div., Oak Ridge Natl. Lab., PO Box Y, Oak Ridge, TN, 37830**
**Environ Mutagen; 3(1):85-89 1981**

Association between altered repair of radiation-induced damage in lymphocytes from two individuals with Down syndrome (trisomy 21) compared with normal cells, and the involvement of the association in increasing chromosome aberration frequencies, were studied. Aberration frequencies in normal and Down lymphocytes were compared following x-irradiation and postirradiation incubation with cytosine arabinoside (ara-C), 5 x 10(-5) M, for 0, 0.5, 1 or 2 hr. Unstimulated Down lymphocytes are more sensitive to the induction of dicentric and ring aberrations by x-rays than normal lymphocytes. X-irradiated cells incubated with ara-C exhibited large increases in aberration frequencies which were proportional to length of exposure to ara-C. Results suggest that the initiation of the repair of damage which is converted into chromosome aberrations is more rapid in Down cells than in normal cells. This could be explained if the total amount of DNA damage which can be converted int aberrations is the same in both cell types but the repair is more rapid in Down cells. Results explain the increased sensitivity of unstimulated lymphocytes from individuals with Down syndrome to the induction of dicentrics by x-rays. The more rapid repair of Down cells results in a higher probability of producing chromosome aberrations and higher aberration frequencies in Down than normal cells. (5 Refs)

### 14. RADIOSENSITIVITY OF FIBROBLASTS FROM PATIENTS WITH RETINOBLASTOMA AND CHROMOSOME-13 ANOMALIES.

**Ejima Y, Sasaki MS, Utsumi H, Kaneko A, Tanooka H**
**Radiation Biology Center, Kyoto Univ., Yoshida-Konoecho, Sakyo-ku, Kyoto 606, Japan**
**Mutat Res; 103(2):177-184 1982**

Cultured fibroblast strains were established from skin biopsies from 14 patients with retinoblastoma (RB) and 5 non-RB patients with inborn chromosome-13 anomalies, and their sensitivities to cell killing by x-rays were compared with those of similarly established cell lines from 7 normal, healthy (N) persons and a patient with ataxia telangiectasia (AT), which represented the radiosensitive reference strain. Cells grown in antibiotic and serum-supplemented alpha-modified minimal essential medium were subjected to a dose of 1,500 rad/min of soft x-rays, except the AT cells, which received 810 rad/min. The cells from the AT patient showed marked sensitivity compared to N cells, but those from RB patients exhibited no radiosensitivity. Cells from 4/5 sporadic RB cases in the sample actually showed resistance to x-ray. The cells of non-RB patients with chromosome-13 anomalies were slightly radiosensitive at lower x-ray doses, but otherwise were not more radiosensitive than N cells. Neither the radiosensitivity of RB nor the presence of a repair locus on chromosome-13 is supported by the present results. (26 Refs)

### 15. POISSON GOODNESS-OF-FIT TESTS FOR RADIATION-INDUCED CHROMOSOME ABERRATIONS.

**Merkle W**
**Institut fur Strahlenschutz, Gesellschaft fur Strahlen- und Umweltforschung, D-8042 Neuberberg, W. Germany**
**Int J Radiat Biol; 40(6):685-692 1981**

Asymptotic and exact Poisson goodness-of-fit tests have been reviewed with regard to their applicability in analyzing distributional properties of data on chromosome aberrations. It has been demonstrated that for typical cytogenetic samples, ie when the av number of aberrations per cell is smaller than one, results of asymptotic tests, especially of the most commonly used u-test, differ greatly from results of corresponding exact tests. While the u-statistic can serve as a qualitative index to indicate a tendency towards under- or over-dispersion, exact tests should be used if the assumption of a Poisson distribution is crucial, eg in investigating induction mechanisms. If the main interest is to detect a difference between the mean and the variance of a sample it is furthermore important to realize that a much larger sample size is required to detect under-dispersion than it is to detect over-dispersion. (Author abstract) (20 Refs)

### 16. SECONDARY CHROMOSOME ABNORMALITIES IN ACUTE NON-LYMPHOCYTIC LEUKAEMIA (MEETING ABSTRACT).

**Golomb HM**
**Department of Medicine, University of Chicago, Chicago, IL**
**Sixth Meeting of the International Society of Haematology, European and African Division, August 30-September 4, 1981, Athens, Greece. Hellenic Society of Haematology 409 pp., 1981.**

Chromosome abnormalities of a clonal nature can be found in approx 50% of patients with acute non-lymphocytic leukemia (ANLL). The presence of a chromosomal abnormality is associated with a worse prognosis in all cases, except if a t(8;21) is present without an associated loss of a sex chromosome. Patients with acute myelocytic leukemia (AML) (M1 and M2) with only abnormal metaphases (AA) have the worst prognosis among ANLL patients whereas AML (M1 and M2) patients with only normal metaphases (NN) have the best prognosis among ANLL patients. The t(8;21), found in approx 8% of patients with ANLL, has been shown to be associated exclusively with AML of the M2 type. The acute leukemia associated with a t(8;21) and a missing sex chromosome is an especially aggressive type. A t(15;17) is present in approx 50% of patients with either hypergranular (M3) or microgranular (M3 variant) promyelocytic leukemia and in no other types of ANLL. Patients with this abnormality seem to have a worse prognosis than patients with M3 or the M3 variant who have a normal karyotype or another karyotypic abnormality. In patients who develop acute leukemia after previous cytotoxic or radiation therapy for a primary malignancy (usually malignant lymphoma or multiple myeloma), clonal chromosome abnormalities are almost always present. The finding of a chromosomal abnormality in a previously treated cancer patient with an isolated cytopenia or pancytopenia is diagnostic or a preleukemic phase. The specific abnormalities found in the majority of patients with second malignancies, such as loss of a No 5 or No 7, as well as the hypodiploid state are found in approx 25% of all aneuploid patients with ANLL de novo. (no Refs)

### 17. ISOLATION AND PARTIAL CHARACTERIZATION OF MUTAGEN-SENSITIVE AND DNA REPAIR MUTANTS OF CHINESE HAMSTER FIBROBLASTS.

**Schultz RA, Trosko JE, Chang CC**
**(c/o Trosko) Dept. Pediatrics and Human Development, Coll. Human Medicine, Michigan State Univ., East Lansing, MI, 48824**
**Environ Mutagen; 3(1):53-64 1981**

Isolation and partial characterization of several mutants of Chinese hamster cells, which are affected in their ability to repair DNA damage or in their sensitivity to radiation or chemical mutations, are discussed. Cells of a subclone of the V79 aneuploid cell line were mutagenized by combined treatment with 5-bromodeoxyuridine and blacklight, followed by UV irradiation. 3H-thymidine was incorporated in repair-proficient cells at high temperature (38.5 C) following UV damage. Cells were held in the cold (4.0 C) to induce radioactive thymidine killing. Repair-deficient and UV-sensitive cells which had survived and formed colonies at low temperature (34.0 C) were tested for recovery. Seventy-two surviving colonies were isolated from 2 x 10(7) cells plated for selection. Four colonies were selected for extensive study. Colony UVs-7 was slightly more sensitive to UV, but not sensitive to x-rays or N-acetoxy-2-acetylaminofluorene (NAc-AAF); this mutant exhibited a highly reduced level of unscheduled DNA synthesis (UDS), as compare to the parental line. UVs-40 and UVs-44 line colonies were sensitive to UV, x-ray, N-methyl-N-nitro-N-nitrosoguanidine, and NAc-AAF, but exhibited normal UDS. Line UVr-23 had enhanced UDS, was resistant to UV, but exhibited no difference in sensitivity to x-ray or NAc-AAF. These four mutants are all stable, and may be useful for the study of mammalian DNA repair processes and mechanisms of mutagenesis. (38 Refs)

### 18. QUANTITATION OF CYCLOBUTANE PYRIMIDINE DIMER FORMATION IN DOUBLE- AND SINGLE-STRANDED DNA FRAGMENTS OF DEFINED SEQUENCE.

**Gordon LK, Haseltine WA**
**Dept. Pathology, Sidney Farber Cancer Inst., 44 Binney St., Boston, MA, 02115**
**Radiat Res; 89(1):99-112 1982**

Dose-response curves for the formation of cyclobutane pyrimidine dimers following irradiation with ultraviolet light were determined. It was found that the rate and extent of dimer formation was determined principally by the two nucleotides which comprised the dimer and that secondary effects were related to the identity of the two nucleotides that flank the dimer. The extent of dimer formation at a potential dimer site is a function of dose and reaches a steady-state level for all dimers at doses above 2000 Joule/square meter (m2). Rates of dimer formation and the steady-state levels are similar in single-and-double stranded DNA. Dose rates of irradiation do not affect the distribution of pyrimidine dimers over the range of 1.8-7.5 Joule/m2/sec. The quantitative data presented provide some general rules for estimating the frequency of cyclobutane pyrimidine dimer formation in heteropolymeric DNA sequences. If the pyrimidine dimer is the primary mutagenic lesion, rules could be applied to predict ultraviolet light-induced mutation frequencies in known sequences of DNA. (23 Refs)

### 19. CELLULAR MOLONEY MURINE SARCOMA (C-MOS) SEQUENCES ARE HYPERMETHYLATED AND TRANSCRIPTIONALLY SILENT IN NORMAL AND TRANSFORMED RODENT CELLS.

**Gattoni S, Kirschmeier P, Weinstein IB, Escobedo J, Dina D**
**Div. Environmental Sciences, Inst. Cancer Res., Columbia Univ., New York, NY, 10032**
**Mol Cell Biol; 2(1):42-51 1982**

The extent of methylation of the oncogenic v-mos sequence of Moloney murine sarcoma virus and its homologue present in normal cells of various vertebrate species (c-mos) was investigated. Results indicated that normal development and differentiation, prolonged serial passage, or transformation (either spontaneous or induced by radiation, chemical carcinogens, or polyoma virus) are not associated with gross rearrangements of the endogenous c-mos sequences in cellular DNA. The c-mos sequence does not contain any intervening sequences and is practically identical to the v-mos sequence. C-mos was not transcribed into RNA in any cells studied. These studies do not rule out the possibility that transient expression of c-mos sequences did occur during early transformation, or that other cellular oncogenic genes might play a role in cell transformation induced by chemical carcinogens or radiation. (43 Refs)

### 20. DNA RADIOSENSITIVITY IN CARCINOMA OF THE HUMAN CERVIX.

**Ono T, Okada S, Iwata M, Ishii H, Hosokawa T**
**(c/o Okada) Dept. Radiation Biophysics, Univ. Tokyo, Hongo, Bunkyo-ku, Tokyo 113, Japan**
**Strahlentherapie; 157(1):33-36 1981**

The radiosensitivity of DNA in human cervix carcinomas was examined by using alkaline sucrose gradient centrifugation to measure radiation-induced single-strand breaks. The DNA strand-break efficiencies observed in DNA of 18 specimens fell into two distinct groups, radiosensitive and radioresistant. The difference in DNA radiosensitivity may be correlated with the pathological classifications of the carcinomas. (Author abstract) (14 Refs)

### 21. EFFECTS OF OXYGEN AND SULPHYDRYL-CONTAINING COMPOUNDS ON IRRADIATED TRANSFORMING DNA. PART I. ACTIONS OF DITHIOTHREITOL.

**Held KD, Harrop HA, Michael BD**
**Dept. Therapeutic Radiology, Mayo Clinic, Rochester, MN, 55901**
**Int J Radiat Biol; 40(6):613-622 1981**

The actions and interactions of oxygen and the sulfhydryl-containing compound dithiothreitol (DTT) upon the radiation sensitivity of the biological activity of purified Bacillus subtilis transforming DNA have been examined. It has previously been shown that the sensitivity of transforming DNA irradiated in dilute solution is less when irradiation is performed in 100% O2 than when in 100% N2, ie O2 protects transforming DNA with a dose-modifying factor of about 0.7. DTT protects transforming DNA in a manner that is dependent on DTT concentration and on gassing conditions. In O2 the DTT protection can largely be attributed to the scavenging of-0H radicals by the DTT, but in anoxia DTT exerts a further protective effect which results in an increasing oxygen enhancement ratio (oer) with increasing DDT concentration to a max oer of about 14 at 2-5 mM DTT. This additional protective effect of DTT is attributable to hydrogen atom donation from DTT to DNA radicals, thus chemically repairing the DNA. Oxygen appears to block this chemical repair reaction. (Author abstract) (23 Refs)

### 22. THE COMBINED ACTION OF X-IRRADIATION, DRUG AND HYPERTHERMIA ON THE DNA IN MAMMALIAN CELLS IN VITRO.

**Djordjevic O, Kostic L**
**Radiological Lab., Inst. Nuclear Sciences 'Boris Kidric', POB 522, 11000 Beograd, Yugoslavia**
**Strahlentherapie; 157(1):46-49 1981**

The effects of the alkylating cytostatic drug PTC on the production of radiation-induced single-strand breaks in DNA, and on the repair in L cells incubated at 37 C or 42 C were studied. The same amount of SSB is obtained when the cells are treated simultaneously with PTC and hyperthermia as when irradiated with 2,500 rad, but different rate in the rejoining was observed. There is no potentiation of SSB formation by pretreatment of cells with 10 ug PTC/ml for 2 hours at 42 C before irradiation, but in these cells less effective repair occurs. The effect of PTC on the rejoining of SSB induced with 2,500 rad depends on the drug's concentration and post-incubation time. (Author abstract) (11 Refs)

### 23. DNA-SYNTHESIZING ACTIVITY IN MOUSE OVARY AFTER X-RAY IRRADIATION.

**Martinova YS, Hadjioloff AI, Kantcheva LS**
**Inst. Morphology, Bulgarian Acad. Sciences, Sofia, Bulgaria**
**Dokl Bolg Akad Nauk; 34(7):1001-1004 1981**

Effect of x-rays on DNA synthesis in ovarian cells was studied in BALB/c mice. The animals were subjected to a single irradiation with 250 or 500 rads. On days 2, 5 and 9 after irradiation mice were injected ip with 3H-thymidine, and the ovaries were examined autoradiographically. The degree of inhibition of DNA synthesis in the follicular cells depended upon the size of the follicle and the dose of irradiation. (11 Refs)

### 24. ELIMINATION OF RADIATION-INDUCED CHROMOSOME ABERRATIONS IN A CULTURE OF HUMAN PERIPHERAL BLOOD LYMPHOCYTES. I. FREQUENCY OF ABERRATIONS IN THE FIRST AND IN THE SECOND MITOSES.

**Piatkin EK, Nugis VIu**
**Inst. Biophysics, Moscow, USSR**
**Tsitologiia; 23(11):1310-1316 1981**

The frequency of radiation-induced chromosome aberrations was studied in human peripheral blood lymphocytes irradiated with 60Co gamma rays (100-500 rads). Irradiated cells were incubated with broxuridine for 58-66 hr, and the chromosome aberrations in the first and second mitoses were assessed by the harlequin staining. For all radiation dosages tested, the frequency of chromosome aberrations in the first mitosis was 1.6-2x greater than that in the second mitosis. (15 Refs) (In RUS)

## OTHER CELLULAR EFFECTS OF IRRADIATION

### 25. HUMAN MONOCYTES AND LYMPHOCYTES DIFFER IN THE RATE OF DNA REPAIR SYNTHESIS AND VIABILITY AFTER EXPOSURE TO NITROGEN MUSTARD.

**Lewensohn R, Ringborg U**
**Radiumhemmet, Karolinska Hosp., Stockholm, Sweden**
**Acta Med Scand; 210(5):381-387 1981**

Unscheduled DNA synthesis was studied in human lymphocytes and monocytes after treatment with nitrogen mustard, methyl-methane-sulfonate and ultraviolet irradiation. The unscheduled DNA synthesis was about 4x higher in monocytes than in lymphocytes after treatment with nitrogen mustard. Treatment with methyl-methane-sulfonate or ultraviolet irradiation confirmed the higher capacity for unscheduled DNA synthesis in the monocytes. When Ficoll-Isopaque-isolated mononuclear cells were exposed to various doses of nitrogen mustard and incubated for different periods, a dose- and time-dependent increase in trypan blue uptake was found. Furthermore, a corresponding dose- and time-dependent decrease was noted in 3H-uridine incorporation. Since trypan blue uptake will not enable differentiation between monocytes and lymphocytes appearing as a mixed cell population, 3H-uridine flash labeling index was studied after exposure to nitrogen mustard. There was a dose- and time-dependent decrease in 3H-uridine labeling index, suggesting a correlation between the absence of 3H-uridine incorporation and increase in trypan blue uptake. When compared to monocytes, the lymphocytes were more affected in this respect after exposure to nitrogen mustard. The possibility that differences in cytotoxic effect may be related to DNA repair mechanisms is discussed. (Author abstract) (34 Refs)

### 26. DELAYED INDUCTION OF ORNITHINE DECARBOXYLASE IN MOUSE SKIN AFTER IRRADIATION WITH BETA-RAYS.

**Fujiki H, Mori M, Tanooka H**

**National Cancer Res. Inst., Tsukiji 5-1-1, Chuo-ku, Tokyo 104, Japan**

**Cancer Lett; 15(1):15-17 1982**

Delayed increase of ornithine decarboxylase (ODC) activity in mouse skin after irradiation with 90Sr-90Y beta rays was studied. Female 8-wk-old CD-1 mice were used in all experiments. The hair on their backs was clipped and further removed 2-3 days before irradiation. The shaved area was irradiated with beta-rays from the 90Sr-90Y source plated on 2-cm diameter metal disk for 13 min at a dose of 230 rad/min on the surface of the skin. Total irradiation dose was 3 kilorad. ODC activity for untreated mice was 0.01 nanomole CO2/30 min/mg protein. The ODC activity remained at the control level until day 14 and then increased to max on about day 17; ODC activity decreased after that, reaching the starting level on about day 20. The visible acute skin reaction was also delayed, reaching max on day 16-20. Beta rays differ from tumor promoters and carcinogens in causing delayed ODC induction. Results indicate that beta rays induce a phenotypic change associated with tumor promotion. (7 Refs)

### 27. AN APPARENT CORRELATION BETWEEN THE INHIBITION OF INDUCED ORNITHINE DECARBOXYLASE ACTIVITY BY GAMMA RADIATION AND THE CAPACITY FOR DNA REPAIR SYNTHESIS IN NORMAL AND ATAXIA TELANGIECTASIA HUMAN FIBROBLASTS: NO CORRELATION WITH CELL SURVIVAL.

**Ben-Hur E, Kol R, Heimer YM, Shiloh Y, Tabor E, Becker Y**

**Dept. Radiobiology, Nuclear Res. Centre-Negev, P.O. Box 9001, Beer-Sheva, Israel**

**Radiat Environ Biophys; 20(1):21-28 1981**

The effects of gamma radiation on induced ornithine decarboxylase (ODC) activity, DNA repair synthesis (DRS), and cell survival were studied in vitro in fibroblasts from normal individuals and patients with ataxia telangiectasia (AT). ODC activity in nonirradiated human fibroblasts was induced after a lag period of 2-3 hr by addition of fresh medium and reached a peak at 7-8 hr. A dose of 108 kilorad (krad) gamma radiation before induction substantially reduced ODC activity in normal cells of strain F107 and AT cells of strains F182 and F184. Cells of strain F196, from an apparently normal individual, showed much greater sensitivity than the other strains. F107 and AT cells showed an inhibition of DRS paralleling the decrease in induction of ODC. F196 cells showed a greater reduction in DRS capacity paralleling their greater inhibition of ODC induction. F107 and F196 showed similar cell survival curves after gamma irradiation (D37 values being 150 +-7 and 135 +-6 rad, respectively). AT cells were more sensitive than normal cells (D37 being 60 +-2 rad for F182 and 45 +-2 rad for 184). Apparently sensitivity of ODC induction and DRS are related, possibly in a causal manner, in normal and AT human fibroblast; cell survival is apparently not related to either ODC induction or DRS. (19 Refs)

### 28. RADIOSENSITIVITY OF STROMAL PROGENITOR CELLS (CFU-F) IN BONE MARROW OF PATIENTS WITH HEMOBLASTOSES.

**Kolesnikova AI, Domracheva EV, Konopliannikov AG, Khoptynskaia SK, Kaplan VP, Vorob'ev AI**
**Inst. Medical Radiology, Obninsk, USSR**
**Probl Gematol Pereliv Krovi; 26(11):37-39 1981**

Comparative radiosensitivity of stromal colony-forming units (CFU-f) isolated from the bone marrow of the patients with acute leukemia, chronic myelosis, myeloma, and lymphosarcoma was studied. Bone marrow suspension was irradiated with 60Co gamma rays at 100 rads/min. After 10-11 days of culturing, the cells were fixed and av diameter of the colonies was measured. Analysis of the dose-effect curves showed that the radiosensitivity of CFU-f in the patients with hematological disorders did not differ from that in healthy controls. (2 Refs) (In RUS)

## THEORETICAL ASPECTS OF RADIATION CARCINOGENESIS

### 29. CONSIDERATIONS ON THE TIME FACTOR IN RADIOBIOLOGY.

**Rossi HH**
**Radiological Res. Lab., Dept. Radiology, Cancer Center/Inst. Cancer Res., Columbia Univ. Coll. Physicians and Surgeons, New York, NY, 10032**
**Radiat Environ Biophys; 20(1):1-9 1981**

The effects of the radiation time factor on carcinogenesis are discussed. In autonomous cells (those that respond only to energy absorbed within them) radiation produces three types of e vents: (1) Class 0 events have influence on effect probability, (2) Class 1 events each singly produce effect (intratract lesions), and (3) Class 2 events produce influence, but do not directly cause an effect. Class 2 events produce intertract lesions. At low doses Class 1 events are more probable than Class 2 events. Experimental evidence indicates that reduction of dose rate reduces the carcinogenic effectiveness of gamma radiation, but increases that of neutron radiation. In general, extension of irradiation doses decreases or increases radiation effectiveness, depending on whether the dose-effect curve is positive or negative. If the sensitivity of a system remains constant, and complete repair occurs between dose fractions, a dose D, applied in n fractions, should produce the effect np1(D/n), where p1(D/n) is the effect of a single dose D/n. Although alterations of sensitivity in autonomous cells must occur by intracellular mechanisms, when low dose neutron irradiation produces altered sensitivity in carcinogenesis, the mechanisms must be intercellular actions that decrease with time. Identification of processes induced by radiation are important to understanding radiation carcinogenesis. (18 Refs)

### 30. A NEW PROTOCOL AND ITS RATIONALE FOR THE STUDY OF INITIATION AND PROMOTION OF CARCINOGENESIS IN RAT LIVER.

**Potter VR**
**McArdle Lab. Cancer Res., Univ. Wisconsin Medical Sch., Madison, WI, 53706**
**Carcinogenesis; 2(12):1375-1379 1981**

A new protocol for carcinogenesis in rat liver is described in order that confirmatory experiments might be undertaken concurrently. The basic protocol, designated IPI (initiator plus promoter plus initiator), is presented in several alternative forms including the possible use of x-irradiation as the initiator. The rationale is discussed in terms of the two-hit somatic mutation theory of Armitage and Doll, with an initial hit produced by the first dose of initiator and expansion of single cells to sizable clones by promotion thereby increasing the probability of a second hit by the second dose of initiator. The question of relevant mutations is taken up and it is proposed that genes for chalones and for chalone receptors are logical targets for consideration in a two-mutation sequence. (Author abstract) (33 Refs)

## ENVIRONMENTAL RADIATION AND PROTECTION STANDARDS

### 31. RADIOACTIVE EMISSIONS AND RADON.

**Harley JH**
**Environmental Measurements Lab., United States Dept. Energy, New York, NY**
**Bull NY Acad Med; 57(10):883-896 1981**

Man is presently exposed to both natural and enhanced sources of radon and its daughters. In both cases, indoor concentrations are much higher than those outdoors and control the total exposure. Sizeable groups live with enhanced levels that are perhaps one tenth of the present occupational limits. This is quite different than with other sources of environmental radiation exposure. Also, unlike other radiation exposures, infants should not be more sensitive than adults. Lung cancer seldom appears before age 40, and the contribution from radon daughter exposure in infancy should be minimal. The lung cancer rate in nonsmokers allows us to put an upper limit on the risk factor relating lung cancer incidence to radon daughter exposure. Considering that not all of the cancers in nonsmokers can be due to radon, a value of 0.002 for the lifetime risk of radon daughter exposure at 1/4 WLM per year fits in with all the data. Since permissible exposure limits are being suggested at levels that may be exceeded in some homes with only natural contributions of radon, any future regulatory action may become difficult to justify. Any given radon daughter concentration presents the same risk whether it is enhanced or natural, and the government agencies involved will be facing many difficult, it not insoluble, problems. (Author abstract) (19 Refs)

### 32. COMPARATIVE FOOD-CHAIN BEHAVIOR AND DISTRIBUTION OF ACTINIDE ELEMENTS IN AND AROUND A CONTAMINATED FRESH-WATER POND.

**Garten CT, Trabalka JR, Bogle MA**
**Oak Ridge Natl. Lab., Oak Ridge, TN**
**Proceedings of the International Symposium on Migration in the Terrestrial Environment of Long-Lived Radionuclides from the Nuclear Fuel Cycle, held in Knoxville, TN, July 27, 1981. Available from National Technical Information Service, Springfield, VA, as DE81026522:, 21 pp., 1981.**

The bioaccumulation of exp 233 exp 234 U, exp 238 U, exp 238 Pu, exp 239 exp 240 Pu, exp 241 Am, and exp 244 Cm in both native and introduced biota was studied at Pond 3513, a former low-level radioactive waste settling basin at Oak Ridge National Laboratory. This system, which was decommissioned in 1976 after more than 30 yr use, contains approx 5 Ci of exp 239 exp 240 Pu; inventories of other actinide isotopes are considerably less. Significantly higher concentrations of actinides in fish that were allowed access to sediments indicated that sedimentary particulates may be the primary source of transuranics to biota in shallow fresh-water ecosystems. Our study determined habitat, in particular the degree of association of an organism with the sediment-water interface, to be the primary factor in controlling transuranic concentrations in aquatic biota. In most of the biological samples analyzed, excluding samples suspected of being contaminated by sediment, exp 241 Am/exp 239 Pu, exp 244 Cm/exp 239 Pu, and exp 238 U/exp 239 Pu ratios were greater than the respective ratio in sediment while exp 233 exp 234 U/exp 238 U, and U, and exp 239 exp 240 Pu/exp 238 Pu ratios were not different from the respective ratios in sediment. The relative uptake of actinides from contaminated sediment by aquatic and terrestrial biota at this site was U greater than Cm greater than or equal to Am greater than Pu. The relative extractability of actinides from shoreline sediment was U greater than Cm approx = Am greater than Pu; we also observed the same relative ranking of sediment-water exchange in situ. Concentrations of transuranics in water, terrestrial vegetation, and vertebrate carcasses were less than 10% of the recommended public exposure maximum permissible concentration of the ICRP. (Author abstract)

### 33. CONCENTRATIONS OF RADIONUCLIDES IN REEF AND LAGOON PELAGIC FISH FROM THE MARSHALL ISLANDS.

**Noshkin VE, Eagle RJ, Wong KM, Jokela TA, Brunk JL**
**California Univ., Berkeley, CA**
**Concentrations of Radionuclides in Reef and Lagoon Pelagic Fish from the Marshall Islands. Available from National Technical Information Service, Springfield, VA, as DE81026319:, 65 pp., 1981.**

A radiological survey was conducted from September through November of 1978 to assess the concentrations of persistent man-made radionuclides in the terrestrial and marine environments of 11 atolls and 2 islands of the Northern Marshall Islands. The atolls and islands include Rongelap, Utirik, Taka, Bikar, Rongerik, Ailinginae, Likiep, Jemo, Ailuk, Mejet, Wotho, Ujelang and Bikini. Over 4,000 terrestrial and marine samples were collected for radionuclide analysis from 76 different islands. Soils, vegetation, indigenous animals, and cistern and groundwater were collected from the islands. Reef fish, pelagic species, clams, lagoon water, and sediments were obtained from the lagoons. A report is given of all available concentration data for exp 137 Cs, exp 90 Sr, sup 239 + 240/Pu, exp 238 Pu, exp 241 Am as well as naturally occurring exp 40 K and other gamma emitting radionuclides in tissue and organs of different species of fish collected from the atolls. (Author abstract)

### 34. COMPARISON OF THE SUBCELLULAR DISTRIBUTION OF MONOMERIC 239PU AND 59FE IN THE LIVER OF RAT, MOUSE, AND SYRIAN AND CHINESE HAMSTERS.

**Winter R, Seidel A**
**Institut fur Genetik und fur Toxicologie von Spaltsoffen, D 7500 Karlsruhe 1, W. Germany**
**Radiat Res; 89(1):113-123 1982**

Four animal species (rat, mouse, Syrian and Chinese hamsters) were tested to determine the subcellular distribution of 239Pu and 59Fe in the liver 10 days following intravenous injection as citrate complexes. In all species 239Pu was bound predominantly to structural elements of the cell several days after its uptake by the liver. The mitochrondria, the endoplasmic reticulum and the pericellular membranes in the liver can probably be excluded as major binding sites for monomeric 239Pu. The role of iron-binding components in the final desposition of the nuclide needs to be elucidated by further studies. The results do not support the assumption that 239Pu is bound to the same structures as iron 10 days after its injection. In rats and mice and to a lesser extent also in Syrian hamsters, lysosomes which are characterized by the prescence of acid phosphatase and aryl sulfatase and the uptake of Triton WR 1339, are important storage organelles. The evidence for lysosomal association is strong in the species which rapidly eliminate 239Pu but equivocal in those which retained 239Pu longer. It is unclear whether these are fundamental differences between animal species in the ways in which transuranium elements are handled in the liver. (15 Refs)

### 35. CANCER RISKS IN PEDIATRIC NUCLEAR MEDICINE (MEETING ABSTRACT).

**Swanson MA, Hines HH**
**University of California Davis Medical Center, Sacramento, CA**
**Clin Nucl Med; 6(9S):448 1981**

Because of pediatricians' interest in long term effects of radiation in childhood, the authors have prepared cancer risk estimates for three more commonly ordered pediatric scans and compared them with the spontaneous incidence of the same cancers in the unexposed population. Calculations were based on age, weight and scan dose, assuming an average life expectancy of 70 years. The BEIR III linear-quadratic model was used to estimate 30 year leukemia and bone cancer risk and the BEIR III linear model for the lifetime risk of hepatic neoplasms. Absorbed dose estimates were taken from the literature for cancer risk calculations. (no Refs)

## REVIEWS AND OTHER STUDIES

### 36. INFLUENCE OF IN VITRO IRRADIATION UPON LIF PRODUCTION BY CONA STIMULATED MONONUCLEAR CELLS.

**Sandru G, Veraguth P**
**Lab. Radiobiology, Dept. Radiotherapy, Univ. Berne, Inselspital, 3010 Berne, Switzerland**
**Int J Radiat Oncol Biol Phys; 7(12):1679-1683 1981**

The effect of in vitro irradiation on production of leukocyte migration inhibitory factor (LIF) by lymphocytes stimulated with Concanavalin A (ConA) was studied. Human mononuclear cells (MNC) from healthy individuals were cultured with or without 90 min pulse exposure to 80 ug ConA/ml. MNC cultures were exposed to irradiation (150 to 1,200 rads within 30 min) before or after exposure to ConA. Irradiation before or after ConA stimulation did not impair LIF production compared to that of non-irradiated MNC. Irradiation produced moderate but significant increases in LIF production in some cultures, mainly those from donors showing poor LIF release after ConA stimulation. MNC culture supernatants that were pretreated with rabbit anti-LIF antibodies had no inhibitory effect on migration of human granulocytes or guinea pig peritoneal exudate cells, indicating the specificity of LIF. Radioresistance of LIF stimulation suggests that LIF production does not require cell proliferation. The increase of LIF production in irradiated MNC cultures suggests that a suppressor-cell population exists that is radiosensitive. Results of the study have implications for immune changes in patients undergoing radiotherapy. (28 Refs)

### 37. CELLULAR TRANSFORMATION BY RADIATION: INDUCTION, PROMOTION, AND INHIBITION.

**Borek C**
**Radiological Res. Lab., Cancer Center/Inst. Cancer Res., Columbia Univ. Coll. Physicians and Surgeons, New York, NY, 10032**
**J Supramol Struct Cell Biochem; 16(4):311-336 1981**

Steps and factors in radiation transformation are reviewed. Recent and current studies using mammalian cell cultures are described: subjects include oncogenic transformation (TR) of animal cells in vitro, quantitative studies in radiation TR, modification of TR by the protease inhibitor antipain, nutritional factors such as retinoids, and thyroid hormone as a modulator of carcinogenesis. Oncogenic TR of human cells in vitro is discussed. (61 Refs)

### 38. AN EPIDEMIOLOGICAL BASIS FOR CANCER CONTROL.

**Armstrong B**
**NH and MRC Res. Unit in Epidemiology and Preventive Medicine, Univ. Western Australia, Dept. Medicine, Nedlands, Australia**
**Cancer Forum; 5(3):136-143 1981**

Primary and secondary prevention of cancer, particularly cancer of the lung, breast, and colon and melanoma, which together account for greater than 40% of new cancer cases and premature mortality is discussed. Primary prevention aims at preventing cancer from occuring by ending exposure to the causal agent either by environmental or life type control. Lung cancer is attributable mainly to cigarette smoking; some cases result from occupational exposure. Breast cancer is associated with nulliparity, first full-term pregnancy at a comparatively late age, low parity, diet, radiation, post-menopausal estrogens, and oral contraceptives. Colon and rectal cancer are mainly related to dietary fiber deficiency and excess fat and meat consumption. Melanoma of the skin is due to exposure to UV radiation. Etiologies of other neoplasms are discussed: brain neoplasms (phenobarbitone use), prostate cancer (diet, cadmium exposure), stomach cancer (diet), leukemia (x-rays, benzene exposure, antineoplastic agent use), pancreatic cancer (diet, cigarette smoking), bladder cancer (occupational exposure to aromatic amines, cigarette smoking), and cervix cancer (sexual promiscuity). Dietary modification, cessation of smoking, and avoidance of excessive exposure to UV light was recommended. Screening methods involved in the secondary prevention of cancer include cervical cytology, proctosigmoidoscopy, and mammography at regular intervals for certain segments of the population. The choice between primary and secondary prevention of cancer is discussed. (20 Refs)

### 39. HEALTH EFFECTS OF COMBINED EXPOSURES IN THE WORK ENVIRONMENT.

**WHO Expert Committee, McDonald JC, Cho KS, Derban LK, Finklea JF, Kundiev Y, Osman Y, Xuechi G**
**Geneva, Switzerland**
**WHO Tech Rep Ser (662): 76 pp., 1981.**

Theoretical aspects of combined effects and current information on occupational exposure, including the results of animal experiments, studies in human beings, and epidemiological field studies are reported. The role of combined exposures in major areas such as occupational mental health, chronic toxicity, parasitic disease, respiratory disease, cancer, and reproductive disorders is presented. Implications for occupational health practice are reviewed and recommendations for research are given. (272 Refs)

### 40. EPIDEMIOLOGY OF CUTANEOUS MALIGNANT MELANOMA.

**Balda BR**
**Dermatologische Klinik und Poliklinik der Universitat, Frauenlobstr. 9-11, D-8000 Munchen 2, W. Germany**
**MMW; 123(50):1923-1926 1981**

Patterns of occurrence and possible causative factors in cutaneous malignant melanoma (MM) are reviewed. MM occurs in 1.8-28.57/100,000 persons, depending on the geographical area studied. A world-wide increase in incidence has been reported with rates increasing as much as 340% in 12 yr. MM occurs most frequently during middle age. Women are affected approx twice as often as men. Survival time after diagnosis is longer for women, however; this may be because MM of the trunk occurs most often in men. Approx 40% of MM carry estrogen receptors, suggesting that hormonal influences affect the incidence and progression of the disease. Avoidance of pregnancy and hormonal contraceptives is therefore recommended for women with MM. Approx 1-7% of MM are related to an autosomal dominant or polygenic factors. In precursor mole syndrome atypical nevi become transformed into MM. A few cases of MM occurring in married couples have been reported that may be due either to infectious factors or to similarities in lifestyle. Ethnic and racial factors affect MM incidence; Celtic or Nordic types showing the highest incidence. Exposure to UV radiation has not been ruled out as a causative factor. Occurrence of MM in locations protected from sunlight suggests that a circulating factor is involved in tumor induction, but no such factor has been demonstrated. (65 Refs) (In GER)

### 41. THE RADIOTOXICOLOGY OF IODINE.

**Taylor DM**
**Inst. Genetics and Toxicology, Kernforschungszentrum Karlsruhe, Postfach 3640, D-7500 Karlsruhe, W. Germany**
**J Radioanal Chem; 65(1/2):195-208 1981**

Toxicology of radioisotopes of iodine is reviewed. Of 30 isotopes, those with mass numbers 123-135 have major radiotoxicological significance. Those with medical applications are 123I, 125I, 131I, and 132I; 129I is a potential environmental hazard. Radiotoxicity (RT) depends on the type of radiation emitted, the half-life of the isotope, and patterns of uptake and retention in the body as a whole and in specific tissues. Induction of benign or malignant thyroid tumors or depression of thyroid function may result from exposure to inorganic 125I or 131I. RT of 131I is greater than that of 125I; 132I, 133I, and 135I, with shorter half-lives, are 10-100x as toxic as 131I. Induction of adrenal, pituitary, and ovarian tumors, parathyroid hypofunction, and other disturbances caused by radioiodine have been demonstrated in animals but not in man. Birth defects and spontaneous abortions in man have not been increased by gonadal doses of up to 800 milligray 131I. RT of organic I-compounds has not been well-studied. Iododeoxyuridine, when labeled with 125I, produces severe and sometimes irreparable damage by Auger electrons when incorporated into DNA. Thyroid carcinoma or adenoma is produced in an estimated 10-20 x 10(-6) persons/Gray/yr by 131I; the risk from mixtures of shorter-lived isotopes may be considerably higher. (50 Refs)

### 42. ETIOLOGICAL FACTORS IN MELANOMA.

**Haim S, Gilhar A**
**No affiliation given**
**Harefuah; 101(5/6):125-126 1981**

The etiology of melanoma is reviewed. Controversies involving theories which implicate exposure to UV radiation, skin color, atmospheric ozone levels, effects of sunlight on the immune system, and estrogen levels are discussed. (33 Refs) (In HEB)

### 43. ASPECTS OF ENVIRONMENTAL INFLUENCES ON MAMMALIAN GONADS WITH PARTICULAR REFERENCE TO TOXIC AGENTS AND ITS IMPLICATIONS FOR HUMAN REPRODUCTION.

**Hilscher W, Hilscher B**
**Abteilung fur Experimentelle Pathologie, Medizinisches Institut fur Umwelthygiene, Universitat Dusseldorf, Dusseldorf, W. Germany**
**Excerpta Med Int Congr Ser; 551:259-268 1981**

Gonadal damage induced by noxious agents within the environment are discussed. Tumors in the gonads induced by noxious agents are rare. Carcinogenic effects of ionizing radiation upon gonadal tissue have not been reported. Studies on the kinetics of female and male germ cells are discussed. (27 Refs)

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# NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

## CHEMICAL CARCINOGENESIS

1. ETHYLENE OXIDE (ETO): EVIDENCE OF CARCINOGENICITY.
Coene RF
National Inst. for Occupational Safety and Health, Cincinnati, OH
Vet Hum Toxicol; 23(6):439-443 1981

## DIETARY FACTORS IN CARCINOGENESIS

2. NUTRITIONAL ASPECTS OF CANCER PREVENTION: AN OVERVIEW.
Silverman J
American Health Foundation, Naylor Dana Inst Disease Prevention, Valhalla, NY, 10595
J Am Vet Med Assoc; 179(12):1404-1409 1981

3. FORMATION OF N-NITROSO COMPOUNDS IN FOODS.
Gray JI
Dept. Food Science and Human Nutrition, Michigan State Univ., East Lansing, MI, 48824
ACS Symp Ser; 174():165-180 1981

## EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

4. LYMPHOMAS AND LEUKAEMIAS. PART 2: TROPICAL AMERICA.
Jimenez E
Hospital Nacional de Ninos 'Dr. Carlos Saenz Herrera', Apartado 1654, San Jose, Costa Rica
Clin Haematol; 10(3):894-915 1981

5. LYMPHOMAS AND LEUKAEMIAS. PART 1: TROPICAL AFRICA.
Olweny CL
Uganda Cancer Inst., P.O. Box 3935, Kampala, Uganda
Clin Haematol; 10(3):873-893 1981

6. MALIGNANT MELANOMA.
Creagan ET
Div. Medical Oncology, Mayo Clinic, Rochester, MN, 55905
Compr Ther; 7(12):36-44 1981

7. MELANOTIC TUMORS OF THE UVEA AND RETINA.
Schmitt H
Universitats-Augenklinik, Theodor-Stern-Kai 7, D-6000 Frankfurt am Main, W. Germany
Med Klin; 76(24):672-675 1981
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## CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

8. THE NATURAL HISTORY OF CARCINOGENESIS: IMPLICATIONS OF EXPERIMENTAL CARCINOGENESIS IN THE GENESIS OF HUMAN CANCER.
Pitot HC, Goldsworthy T, Moran S
McArdle Lab. for Cancer Res., Dept. Oncology, Medical Sch., Univ. Wisconsin, Madison, WI, 53706
J Supramol Struct Cell Biochem; 17(2):133-146 1981

9. CURRENT CONCEPTS AND CONTROVERSIES IN CHEMICAL CARCINOGENESIS.
Weinstein IB
Div. Environmental Sciences, Inst. Cancer Res., Columbia Univ. Coll. Physicians and Surgeons, New York, NY, 10032
J Supramol Struct Cell Biochem; 17(2):99-120 1981

## VIRAL AND IMMUNOLOGICAL ASPECTS OF CARCINOGENESIS

10. BURKITT'S LYMPHOMA.
Ambrus JL, Ambrus CM
Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
J Med; 12(6):385-413 1981

11. PRIMARY HEPATIC CARCINOMA.
Iosquin CJ
Catedra de Medicina Interna A, Facultad de Ciencas Medicas, La Plata, Argentina
Rev Fac Cienc Med La Plata; 4(2):27-31 1981
In SPA

## METHODOLOGY IN CARCINOGENESIS RESEARCH

12. MUTAGENESIS AND CARCINOGENESIS TESTING IN VITRO.
Casto BC
Northrop Services, Incorporated, P.O. Box 12313, Research Triangle Park, NC, 27709
Biotechnol Bioeng; 23(12):2659-2671 1981

## OTHER REVIEWS IN CARCINOGENESIS

13. CANCER IN THE YEAR 2000. A REVIEW.
Saxen E
Suomen Syoparekisteri, Liisankatu 21 B, 00170 Helsinki 17, Finland
Duodecim; 97(20):1708-1716 1981
In FIN

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# RADIATION CARCINOGENESIS

SERIES CK06 No. 82/07

JULY, 1982

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# RADIATION CARCINOGENESIS IN HUMANS

### 1. MORTALITY IN WOMEN TREATED BY HYPERTHYROIDISM.

**Hoffman DA, McConahey WM, Diamond EI, Kurland LT**
**Environmental Epidemiology Branch, NCI, Rm. 3C-07, Landow Bldg., Bethesda, MD, 20205**
**Am J Epidemiol; 115(2):243-254 1982**

To evaluate the late effects of exposure to radioiodine (131I), a retrospective cohort study was conducted of women treated for hyperthyroidism at the Mayo Clinic, Rochester, Minnesota, from 1946 through 1964. Cause of death was determined in 1,005 women treated with 131I and in 2,141 women surgically treated. No increased risk of total mortality was observed for the 131I-treated women (relative risk = 1.0). There were no increased risks for the major causes of mortality (cancer, cardiovascular-renal disease or cerebrovascular lesions) in the 131I-treated women; in addition, there were no increased risks for site-specific cancer mortality. Several hypotheses are presented to suggest reasons for the lack of association between 131I exposure and increased cancer mortality. (Author abstract) (41 Refs)

### 2. SCREENING FOR BREAST CANCER IN A HIGH-RISK SERIES.

**Woodard ED, Hempelmann LH, Janus J, Logan W, Dean P**
**Univ. Rochester Sch. Medicine and Dentistry, P.O. Box 307, 601 Elmwood Ave., Rochester, NY, 14642**
**J Surg Oncol; 19(1):31-35 1982**

A unique cohort of women at increased risk of breast cancer because of prior x-ray treatment of acute mastitis and their selected high-risk siblings were offered periodic breast cancer screening including physical examination of the breasts, mammography, and thermography. Twelve breast cancers were detected when fewer than 4 would have been expected based on age-specific breast cancer detection rates from the National Cancer Institute/American Cancer Society Breast Cancer Demonstration Detection Projects. Mammography was positive in all cases but physical examination was positive in only three cases. Thermography was an unreliable indicator of disease. Given the concern over radiation-induced risk, use of low-dose technique and of criteria for participation that select women at high risk of breast cancer will maximize the benefit/risk ratio for mammography screening. (Author abstract) (12 Refs)

# EXPERIMENTAL RADIATION CARCINOGENESIS

### 3. CELL TRANSFORMATION AS A SYSTEM FOR STUDYING MECHANISMS OF CARCINOGENESIS.

**Kakunaga T, Crow JD, Lo KY, Hamada H, Kirakawa T**
**Cell Genetics Section, Lab. Molecular Carcinogenesis, NCI, NIH, Bethesda, MD, 20205**
**Gann Monogr Cancer Res; 27:231-242 1982**

Molecular evidence of mutation occurrence in a chemically-transformed cell is presented. The value and concept of an in vitro mammalian cell transformation system for studying carcinogenesis is discussed. Six subclones of BALB/3T3A31 cells which showed constant susceptibility to induced transformation through more than 50 cell generations were highly susceptible to UV irradiation (A31-1-13), intermediately sensitive (A31-1-1, A31-1-2, and A31-1-7), and resistant (A31-1-8 and A31-1-15). These cell variants were examined for the killing effects of carcinogens, transformation induction by chemical carcinogens, transformation by tumor viruses, induction of ouabain-resistance mutation, and type and amount of DNA adducts formed after treatment with chemical carcinogens and their rate of removal. The results suggest that mutations or DNA damage induced by carcinogens have nothing to do with transformation induction, or that the transformation process involves two steps: the mutational step and a step required for expression of the transformed phenotype. A procedure for isolating a recombinant DNA containing a DNA sequence complementary to a particular messenger RNA for molecular cloning is described. (38 Refs)

### 4. NEOPLASTIC TRANSFORMATION OF HUMAN DIPLOID FIBROBLASTS TREATED WITH CHEMICAL CARCINOGENS AND CO-60 GAMMA-RAYS.

**Namba M, Nishitani K, Fukushima F, Kimoto T, Utsunomiya J, Hayflick L**
**Dept. Pathology, Kawasaki Medical Sch., Matsushima 577, Kurashiki 701-01, Japan**
**Gann Monogr Cancer Res; 27:221-230 1982**

Transformation of four strains of normal human fibroblasts with repeated treatment with 4-nitroquinoline 1-oxide (4NQO) and two strains with 60Co gamma-rays is reported. Single treatment with those agents had no such effect. A total of 256 experiments were conducted, 116 with 4NQO and 49 with 60Co gamma rays. The transformed cell lines had the following features; epithelial-like morphology, unlimited growth potential, abnormal karyotypes (heteroploid), increased saturation density, reduced growth inhibition by theophylline, increased lactate dehydrogenase isozyme B(H)/A(M) ratio, no large external transformation sensitive protein, elevated colony formation in soft agar, and a low serum requirement for growth. When unlimited growth and abnormal karyotypes are present, neoplastic transformation in human cells is indicated. Criteria of the morphology of transformed colonies were defined. Advantages and disadvantages of using normal human fibroblasts for transformation studies were discussed. Future considerations for the use of normal human fibroblasts for transformation studies were proposed. (21 Refs)

### 5. CARCINOGENIC EFFECTS OF RADON DAUGHTERS, URANIUM ORE DUST AND CIGARETTE SMOKE IN BEAGLE DOGS.

**Cross FT, Palmer RF, Filipy RE, Dagle GE, Stuart BO**
**Biology Dept., Pacific Northwest Lab., Richland, WA, 99352**
**Health Phys; 42(1):33-52 1982**

The development of pulmonary lesions in beagle dogs was studied following chronic inhalation exposures to radon (at 105 +-20 nCi/l), radon daughters (at 605 +-169 WL), uranium ore dust (at 12.9 +-6.7 mg/m3) and cigarette smoke. Chronic exposures to mixtures of these agents caused significant lifespan shortening when compared with controls. Survival times of controls and smoke-exposed dogs were equivalent during the 4 to 5-yr mean survival time of the dogs exposed to radon-daughter and ore-dust mixtures (with or without added cigarette smoke). Animals with tumors of the respiratory tract generally had cumulative radon-daughter exposures exceeding 13,000 WLM, and their survival time was longer than the survival time of nontumor-bearing animals. Under the conditions of the experiment, exposure to cigarette smoke was found to have a mitigating effect on radon daughter-induced tumors. It is uncertain whether this would be a general finding applicable to other levels of exposure to radon daughters, uranium ore dust and cigarette smoke. Exposures to smoke from 10 cigarettes/day, 7 days/wk produced no significant respiratory tract lesions. However, exposure to 20 cigarettes/day, 7 days/wk resulted in pulmonary emphysema, fibrosis and chronic bronchitis and bronchiolitis. Emphysema and fibrosis were much more prevalent and severe in the dogs exposed to mixtures which included radon daughters and uranium ore dust. These dogs also had adenomatous lesions which progressed to squamous metaplasia of alveolar epithelium, epidermoid carcinoma and bronchioloalveolar carcinoma. Pathologic changes in the airways of these dogs were most prominent in the nasal mucosa, and included a few squamous carcinomas in the nasal cavity. We conclude that the beagle dog is a useful animal for modeling pulmonary lesions produced by uranium mine air contaminants. Tumors were produced at levels that did not greatly exceed some exposures reported for uranium miners. These tumors, found after approx 50 mo of exposure, might partially account for the absence of tumors in experiments where exposures terminated before 50 mo. (Author abstract) (33 Refs)

### 6. NODULAR HYPERPLASIA OF THE LIVER IN THE BEAGLE DOG.

**Fabry A, Benjamin SA, Angleton GM**
**Dept. Safety Assessment, Merck Sharp and Dohme Res. Lab. (W44-1), West Point, PA, 19486**
**Vet Pathol; 19(2):109-119 1982**

Gross and light microscopic features of focal nodular hyperplasia of the liver were investigated in beagle dogs used for the study of the long-term effects of low-dose, wholebody, $^{60}Co$ gamma radiation. The nodules were morphologically similar in the irradiated and unirradiated dogs. Microscopically, the normal lobular architecture, although retained, often was distorted. Hepatocytes in the nodules often were vacuolated and the distribution of vacuolated cells varied from focal to diffuse. There were more hepatocytes per unit area within nodules than in the adjacent parenchyma. Nodule hepatocytes were more variable in size. A lower proportion were binucleate and a higher proportion were in mitosis. The cells in the nodules contained less hemosiderin. The incidence of hyperplastic nodules was directly related to age but not to sex, and was higher in irradiated dogs than in controls. Nodular hyperplasia occurred in association with primary hepatocellular neoplasms in only two dogs. (Author abstract) (24 Refs)

### 7. GENETIC COMPONENT IN RAT MAMMARY CARCINOGENESIS.

**Vogel HH, Turner JE**
**Dept. Radiation Oncology, Univ. Tennessee Center for Health Sciences, 800 Madison Ave., Memphis, TN, 38163**
**Radiat Res; 89(2):264-273 1982**

Mammary tumor induction following whole-body irradiation of rats of five different genetic strains was investigated. Female rats were exposed as young adults to 50 rad fission neutron s, with a neutron-to-gamma ratio of about 7. After 1 yr, single mammary tumors were found in 56% of Long-Evans and Sprague-Dawley strains; palpable mammary tumors were found in 25-29% of the Buffalo and Fischer-344 strains, but in only 5% of the Wistar-Lewis strain. Only one tumor was found in 73 unirradiated controls. Mammary tumors appeared much earlier in rats exposed to fission neutrons than in control rats. No evidence was obtained that mammary neoplasms increased with age. The order of sensitivity among the five strains tested and the percentages of rats developing mammary tumors within 1 yr did not change from the first radiation experiments (about 70 days) to the fourth replicate experiment (about 200 days of age). Chi square analysis of tumors induced after 1 yr shows a highly significant strain difference: sensitivity in decreasing order was Long-Evans; Sprague-Dawley; Buffalo; Fischer; and Wistar-Lewis. Most tumors were adenofibromas or fibroadenomas, both benign. The total of all five strains for diagnosed adenocarcinomas in the first yr after irradiation was 36%. Nearly half the mammary neoplasms were first found between days 300 and 365 after exposure. (20 Refs)

### 8. UVR RADIOMETRY OF SOLAR SIMULATED RADIATION IN EXPERIMENTAL PHOTOCARCINOGENESIS STUDIES.

**Young AR, Challoner AV, Magnus IA, Davis A**
**Dept. Photobiology, Inst. Dermatology, Homerton Grove, London E9 6BX, England**
**Br J Dermatol; 106(1):43-52 1982**

The UVR radiometry of a long-term mouse photocarcinogenesis project is described. The methods used were (a) a phototherapy (UV-A) radiometer, (b) an electronic integrating dosimeter, (c) indirect spectroradiometry and (d) polysulphone and phenothiazine film badges for UV-B and UV-A respectively. The merits of the various methods are discussed. All but the phenothiazine film were considered to be satisfactory. The importance of reliable UVR radiometry is emphasized. (Author abstract) (17 Refs)

## EXPERIMENTAL RADIATION MUTAGENESIS

### 9. MUTAGENICITY OF GAMMA-IRRADIATED OXYGENATED AND DEOXYGENATED SOLUTIONS OF 2-DEOXY-D-RIBOSE AND D-RIBOSE IN SALMONELLA TYPHIMURIUM.

**Wilmer J, Schubert J, Leveling H**
**Div. Nutrition and Food Res., TNO, Dept. Biological Toxicology, P.O. Box 360, 3700 AJ Zeist, The Netherlands**
**Mutat Res; 90(4):385-397 1981**

Mutagenic activity (MA) of soln of 2-deoxy-D-ribose (2DDR) and D-ribose (DR) irradiated under different conditions was studied in Salmonella typhimurium strains TA98, TA100, TA1535, TA1537, and TA1538. Metabolic activation was provided by S9 mix prepared from liver homogenates from Wistar rats treated with Aroclor. Test soln were irradiated with gamma-radiation (0.12-0.14 kilogray(kGy)/min; total dose 10 kGy). Before and during irradiation highly purified $O_2$, $N_2$, or $N_2O$ was bubbled through the soln. $H_2O_2$ present in irradiated oxygenated soln showed MA in TA98 and TA1537. MA of $H_2O_2$ was eliminated in the presence of S9. Irradiated soln of 2DDR or DR were mutagenic in TA98 and TA100 but not in the other strains. In the absence of S9, $N_2O$-saturated soln of 2DDR showed greater MA than $N_2$-saturated soln, suggesting that the OH radical is involved in production of mutagenic products of radiolysis. Malonaldehyde (MDA) was not mutagenic at concentrations produced by irradiation. MA of individual products of radiolysis were not determined. MA of irradiated 2DDR soln in TA100 increased with the level of aldehydes other than MDA. MA of irradiated 2DDR soln was reduced in a temperature-dependent manner by heating of the soln, supporting the hypothesis that MA is caused by carbonyl or dicarbonyl compounds. Autoclaved, nonirradiated soln of 2DDR showed no MA in S typhimurium. (22 Refs)

## EFFECTS OF IRRADIATION ON CHROMOSOMES AND DNA

### 10. DNA REPAIR AND MUTAGENESIS OF SINGLE-STRANDED BACTERIOPHAGES.

**Doubleday OP, Brandenburger A, Godson GN, Wagner R, Radman M**
**Rue des Chevaux 67, B-1640 Rhode-St-Genese, Belgium**
**Gann Monogr Cancer Res; 27:3-11 1982**

DNA sequences of revertants of two M13 amber mutants, am6H2 and am7H3, isolated from populations of irradiated and unirradiated phages grown in irradiated or unirradiated host bacteria were analyzed. DNA sequences in the region of the amber mutation were determined. Forty-nine revertants of am6H1 and 125 of am7H3 were sequenced. All detectable single nucleotide changes were seen except the thymine-adenine-guanine (TAG) to GAG change, which was not found for either amber. No obvious specificity of mutagenesis by either UV- or gamma-irradiation of target DNA were seen. No specificity of mutagenesis by an error-prone repair activity (SOS repair system) acting upon either irradiated or unirradiated DNA was revealed, although induction of host SOS repair activity increased revertant yields. Both transitions and transversions, and changes involving each of the three bases of the amber codon were induced by all combinations of host cell and target irradiation. No pattern of revertant sequences was obtained to suggest that pyrimidine dimers are the primary sites of base changes. DNA sequences of revertants isolated from UV-irradiated phage populations demonstrated that pyrimidine dimers are not the main sites of mutations in UV-irradiated DNA. UV-induced mutagenesis may be untargeted or may occur at sites of lesions other than pyrimidine dimers. (23 Refs)

### 11. CYTOGENETIC STUDIES IN PATIENTS PREVIOUSLY TREATED FOR HODGKIN'S DISEASE.

**Lawler SD, Summersgill BM, McElwain TJ**
**Royal Marsden Hosp., Fulham Road, London, SW3 6JJ, England**
**Cancer Genet Cytogenet; 5(1):25-35 1982**

A cytogenetic study was made of bone marrow cells and lymphocytes from patients who had been successfully treated with various regimens for Hodgkin's disease. Most of the patients had been off treatment for at least 3 yr before the study began. They were divided into three groups according to the intensity of the therapy received. The frequency of gaps and breaks in the chromosomes of lymphocytes was above normal limits and similar in the three treatment groups. In contrast, the frequency of both lymphocytes and bone marrow cells with rearranged karyotypes was correlated with the intensity of treatment. Clones of cells with an abnormal karyotype were found in only two patients, both of whom were in the group receiving the most intensive therapy, ie, chemotherapy and total nodal irradiation. (Author abstract) (15 Refs)

### 12. X-RAY-INDUCED CHROMOSOME DAMAGE IN LIVE MAMMALIAN CELLS, AND IMPROVED MEASUREMENTS OF ITS EFFECTS ON THEIR COLONY-FORMING ABILITY.

**Joshi GP, Nelson WJ, Revell SH, Shaw CA**
**Dept. Physics, Inst. Cancer Res., Sutton, Surrey, England**
**Int J Radiat Biol; 41(2):161-181 1982**

We have improved the precision of the technique described by Grote et al for the observation of the radiation responses of live cultured mammalian cells with an incubated phase-contrast microscope: the colony-forming abilities of single cells obtained by selective detachment of mitoses (instead of cell pairs as previously) may now be followed individually and may be directly compared with chromosome damage detected after post-radiation mitosis (M1). An x-ray dose of 1.4 Gy to diploid Syrian hamster cells (BHK 21 C13) in G1 had no effect on cell ability to reach M1. If chromosome fragment loss was then detected (as micronuclei) in the daughter-cell pair then colony-forming ability nearly always deteriorated, and either a stop-growth (79%) or a slow-growth (21%) colony resulted; but chromosomal bridges which persisted beyond M1 broke during interphase 1 and themselves caused no detectable cell damage additional to that attributable to the micronuclei which accompanied them. (Author abstract) (30 Refs)

### 13. THE SENSITIVITY OF ACTIVE AND INACTIVE CHROMATIN TO IONIZING RADIATION-INDUCED DNA STRAND BREAKAGE.

**Chiu SM, Oleinik NL**
**Div. Radiation Biology, Dept. Radiology, Case Western Reserve Univ., Cleveland, OH, 44106**
**Int J Radiat Biol; 41(1):71-77 1982**

Sensitivity of Tetrahymena pyriformis strain GL-C DNA in actively transcribing and inactive states was compared with regard to gamma-radiation-induced single-strand break (SSB) induction. Following electrophoresis on agar gels and hybridization with poly(A+)RNA, nuclear DNA from irradiated cells was found in broader peaks and contained smaller fragments than did control DNA. In unirradiated cells, the profiles of transcribing and bulk DNA were similar, suggesting that transcribing genes are initially randomly distributed in all fragment sizes of nuclear DNA. Transcribing DNA from irradiated cells was found preferentially among the smaller fragments of total DNA. The apparent difference in the behavior of transcribing DNA from unirradiated and irradiated cells was not due to contamination of poly(A+)RNA with ribosomal RNA. The av mol wt of transcribing DNA was slightly but consistently greater than that of total nuclear DNA in unirradiated cells, while the reverse was true for irradiated DNA. When unirradiated nuclear DNA was mechanically sheared into fragment sizes comparable to those from irradiated cells, the similarity of the profiles of chromosomal and transcribing DNA was maintained after reduction of the fragment size of nuclear DNA. In vitro, no differences in the radiation sensitivities of transcribing and chromosomal DNA were observed. Kinetics of SSB rejoining are described. The results indicated that chromatin organization is important in the determination of the sensitivity of cellular DNA towards gamma-radiation. Not only yield but also the rate of repair of SSB is greater in actively transcribing genes than in the total nuclear DNA. (30 Refs)

### 14. X-RAY INHIBITION OF DNA SYNTHESIS AT DISCRETE TIMES DURING S PHASE IN SYNCHRONOUS HUMAN DIPLOID FIBROBLASTS.

**Kapp LN, Painter RB**
**Lab. Radiobiology, Univ. California, San Francisco, CA, 94143**
**Radiat Res; 89(2):424-427 1982**

The incorporation of thymidine into irradiated and unirradiated diploid fibroblasts at various times during S phase was investigated. Results indicated that most replicons initiate during relatively restricted times in S phase. Results support a model of diploid fibroblast S phase that consists of multiple initiations of large numbers of replicons during short, specific times. (12 Refs)

### 15. CHANGES IN THE SUPERCOILED STRUCTURE OF NUCLEAR DNA IN RAT AND HUMAN PERIPHERAL BLOOD LYMPHOCYTES AFTER GAMMA-IRRADIATION.

**Klimov NA, Vashchenko VI, Kolyubaeva SN, Komar VE**
**Central Res. Inst. Rontgenology and Radiology, USSR Ministry Public Health, Leningrad 188646, USSR**
**Int J Radiat Biol; 41(2):221-225 1982**

Damage and repair of DNA as indicated by changes in the supercoiled structure (SCS) of DNA were studied in vitro and in vivo. After exposure to gamma-irradiation DNA showed a relaxation of SCS. Both in vitro and in vivo DNA was repaired in a three-phase process reflecting repair of single-strand breaks, degradation of DNA, and further repair of single-strand breaks. The process was delayed in vivo, suggesting the presence of inhibiting factors. (21 Refs)

### 16. YIELD OF CHROMOSOME ABERRATIONS IN HUMAN LYMPHOCYTES TREATED WITH 5-FLUORODEOXYURIDINE ALONE AND IN COMBINATION WITH GAMMA RADIATION: CHANGES IN THE RESPONSE DURING THE MITOTIC CYCLE.

**Poriadkova NA, Izmailova NN, Luchnik NV**
**Res. Inst. Medical Radiology, Obninsk, USSR**
**Genetika; 17(12):2212-2219 1981**

The chromosome-modifying effect of 5-fluorodeoxyuridine (FDU) was studied in cultured human lymphocytes. The cells were irradiated with 50 or 100 rads and, immediately afterward were placed in medium containing the FDU (2 x 10(-7) M) for 2.5 hr. Cytogenetic analysis showed that exposure of the cells to FDU alone increased the yield of chromosome aberrations at the end of stage G1 and in stage G2. The yield of chromosome aberrations after exposure to FDU in combination with irradiation was similar to that after exposure to either the FDU or the radiation alone. These findings indicate that the pseudomutagenic effect of FDU is associated with the inhibition of repair of spontaneous or radiation-induced aberrations. (27 Refs) (In RUS)

### 17. NOTES ON CYTOGENETIC EFFECTS OF IRRADIATION ON THE OOCYTES AT MEIOTIC STAGES IN THE CHINESE HAMSTER.

**Sonta S**
**Dept. Genetics, Inst. Developmental Res., Aichi Prefectural Colony, Kasugai 480-03, Japan**
**Proc Jpn Acad [B]; 57(7):244-247 1981**

Cytogenetic effects of x-irradiation were studied in meiotic stages of primary oocytes of 24-30-wk-old female Chinese hamsters. Frequency of chromosome aberrations following 200 R x-irradiation is presented (33.8% were structural aberrations represented by fragments and chromatid breaks, 6.3% included numerical aberrations involving heteroploidy and diploidy, and 7.7% included both structural and numerical aberrations). Frequency of oocytes with chromosome aberrations was higher in the group exposed in the late afternoon of the 1-day interval than in other groups. (11 Refs)

### 18. FREQUENCY OF ABERRATIONS IN MONO- AND DI-5-BROMODEOXYURIDINE SUBSTITUTED CHROMATIDS.

**Antoshchina MM, Poriadkova NA, Luchnik NV**
**Res. Inst. Medical Radiology, Obninsk, USSR**
**Genetika; 17(12):2167-2171 1981**

The effect of bromodeoxyuridine (BDU) on chromatid radiosensitivity was studied in cultured Chinese hamster fibroblasts and human lymphocytes. The cells were incubated with the BDU for two cell cycles; at stage G2 of the second mitosis, the cells were irradiated with 60Co gamma rays (40 rads/min, total dose 100 rads). Harlequin staining showed that the number of breaks in light (disubstituted) regions was significantly lower than that in dark (monosubstituted) regions. (8 Refs) (In RUS)

## OTHER CELLULAR EFFECTS OF IRRADIATION

### 19. A MATHEMATICAL MODEL RESOLVING NORMAL HUMAN BLOOD LYMPHOCYTE POPULATION X-RAY SURVIVAL CURVES INTO SIX COMPONENTS: RADIOSENSITIVITY, DEATH RATE AND SIZE OF TWO RESPONDING SUBPOPULATIONS.

**Thomson AE, Vaughan-Smith S, Peel WE**
**Cytochemistry Lab., Imperial Cancer Res. Fund, Lincoln's Inn Fields, London, England**
**Int J Radiat Biol; 41(1):15-32 1982**

The analysis was based on observations of survival decrease as a function of dose (range 0-5 Gy (= 500 rad)) and time after irradiation in vitro. Since lymphocyte survival is also sensitive to culture conditions the effects of radiation were examined daily up to 3 days only, while survival of control cells remained ca. 90%. The time-dependent changes were resolved as the death rates (first-order governed) of lethally-hit cells (apparent survivors), so rendering these distinguishable from the morphologically identical, true (ultimate) survivors. For 12 blood donors the estimated dose permitting 37% ultimate survival (D37 value) average 0.72 +-0.18 (SD) Gy for the more radiosensitive lymphocyte fraction and 2.50 +-0.67 Gy for the less radiosensitive, each fraction proving homogeneously radiosensitive and the latter identifying substantially in kind with T-type (E-rosetting lymphocytes). The half-life of lethally-hit members of either fraction varied widely among the donors (ranges, 25-104 hr and 11-40 hr, respectively). Survival curves reconstructed by summating the numerical estimates of the six parameters according to the theoretical model closely matched those observed experimentally (range in multiple correlation coefficient, 0.9709-0.9994 for all donors). This signified the absence of any additional, totally radioresistant cell fraction. (Author abstract) (28 Refs)

### 20. ALPHA-IRRADIATION-INDUCED G2 DELAY: A PERIOD OF CELL RECOVERY.

**Lucke-Huhle C**
**Kernforschungszentrum Karlsruhe, Institut fur Genetik und fur Toxikologie von Spaltstoffen, Postfache 3640, D 7500 Karlsruhe 1, W. Germany**
**Radiat Res; 89(2):298-308 1982**

Alpha particles with a linear energy transfer of about 110 keV/micrometer were very effective in causing G2 delay in exponentially growing Chinese hamster V79 cells. In contrast to the situation following x-ray or Cobalt 60 gamma irradiation, where even nonsurviving cells can proceed through several mitoses, the damage caused by alpha irradiation at doses higher than 0.5 Gy prevented mitosis in increasing fractions of irradiated cells in a dose dependent manner. It is concluded that the repair process inhibited by caffeine is essential for survival after alpha irradiation, and occurs in G2. (41 Refs)

### 21. ACTION OF X-RAYS AND NEURAMINIDASE ON PINOCYTOTIC ACTIVITY AND MICROTUBULE-MICROFILAMENT SYSTEM OF EHRLICH ASCITES TUMOR CELLS IN MONOLAYER CULTURE.

**Pfab R, Schachtschabel DO, Paul N, Kern HF, Hess F**
**Klinik und Poliklinik fur Strahlentherapie und Rontgendiagnostik, Univ. Marburg, Robert-Koch-Str. 8a, D-3550 Marburg, W. Germany**
**Strahlentherapie; 157(7):468-473 1981**

Monolayer cultures of Ehrlich ascites tumor cells in exponential growth phase were treated with x-rays and neuraminidase alone or in combination. A radiation dose of 2 Gy (200 rad) and higher effected a significant inhibition of DNA synthesis and cell proliferation. Neuraminidase treatment in addition to irradiation did not modify the growth-inhibitory irradiation effect. Cells pretreated for 0.5 to 1.0 hr with neuraminidase (in Earle's salt solution) and cultured thereafter (4 hr) in serum-containing growth medium exhibited an enhanced development of the microtubule-microfilament-system. Morphometric analysis of microtubules on electron-microscopic sections revealed a nearly four-fold increased number in neuraminidase treated cells while the average length of microtubules was similar to controls. Pinocytosis as measured by the ultrastructural uptake of ferritin appeared to be increased following neuraminidase treatment. A connection between neuraminic acid containing components (glycoproteins or glycolipids?) of the cell membrane or cell surface, on the one hand, and the cytoskeleton and the endocytotic process of these tumor cells, on the other hand, is suggested. (Author abstract) (25 Refs) (In GER)

### 22. RADIATION-INDUCED STRUCTURAL CHANGES IN HUMAN ERYTHROCYTE MEMBRANE PROTEINS REVEALED BY SODIUM DODECYL SULFATE/POLYACRYLAMIDE GEL ELECTROPHORESIS.

**Todo T, Yonei S, Kato M**
**Lab. Radiation Biology, Faculty of Science, Kyoto Univ., Kitashirakawa, Sakyo, Kyoto 606, Japan**
**Radiat Res; 89(2):408-419 1982**

Differences in the radiosensitivity of the major proteins of human erythrocyte membranes was investigated. It was determined that disulfide formation is a minor event and more complex reactions are involved in the radiation-induced damage to membrane proteins. Analysis of the proteins by sodium dodecyl sulfate/polyacrylamide gel electrophoresis revealed the appearance of both cross-linked aggregates and radiolytic products of spectrin. Spectrin was the most sensitive of the erythrocyte membrane proteins to x-irradiation. (34 Refs)

## THEORETICAL ASPECTS OF RADIATION CARCINOGENESIS

### 23. MUTATION FREQUENCIES IN MALE MICE AND THE ESTIMATION OF GENETIC HAZARDS OF RADIATION IN MEN.

**Russell WL, Kelly EM**
**Biology Div., Oak Ridge Natl. Lab., Oak Ridge, TN, 37830**
**Proc Natl Acad Sci USA; 79(2):542-544 1982**

Estimation of the genetic hazards of ionizing radiation in men is based largely on the frequency of transmitted specific-locus mutations induced in mouse spermatogonial stem cells at low radiation dose rates. The publication of new data on this subject has permitted a fresh review of all the information available. The data continue to show no discrepancy from the interpretation that, although mutation frequency decreases markedly as dose rate is decreased from 90 to 0.8 R/min (1 R = 2.6 x 10(-4) coulombs/kg) there seems to be no further change below 0.8 R/min over the range from that dose rate to 0.0007 R/min. Simple mathematical models are used to compute: (a) a max likelihood estimate of the induced mutation frequency at the low dose rates, and (b) a max likelihood estimate of the ratio of this to the mutation frequency at high dose rates in the range of 72 to 90 R/min. In the application of these results to the estimation of genetic hazards of radiation in man, the former value can be used to calculate a doubling dose - ie, the dose of radiation that induces a mutation frequency equal to the spontaneous frequency. The doubling dose based on the low-dose-rate data compiled here is 110 R. The ratio of the mutation frequency at low dose rate to that at high dose rate is useful when it becomes necessary to extrapolate from experimental determinations, or from human data, at high dose rates to the expected risk at low dose rates. The ratio derived from the present analysis of 0.33 (Author abstract) (13 Refs)

### 24. INITIATION AND PROMOTION, MUTAGENESIS AND TRANSFORMATION OF C3H/10T1/2 MOUSE EMBRYO FIBROBLASTS.

**Heidelberger C**
**Univ. Southern California Sch. Medicine, Los Angeles, CA, 90031**
**Gann Monogr Cancer Res; 27:207-219 1982**

The C3H/10T1/2 mouse embryo fibroblast cloned cell line is discussed with respect to initiation and promotion, mutagenesis, and transformation. Transformation by polycyclic aromatic hydrocarbons was dose-dependent and did not involve activation of an endogenous retrovirus or its cores or RNA. Metabolism of benzo[a]pyrene in microsomes of these cells involves formation of 7,8-and 9,10-diols, phenols and quinones. UV light is a pure initiator, x-rays initiate transformation, and saccharin in a weak promoter. While 12-O-tetradecanoyl phorbol-13-acetate (TPA) is strongly mitogenic and produces hyperplasia in mouse skin, it does not significantly increase the saturation density of C3H/10T1/2 cells. All chemical classes of tumor promoters are not suitable for screening by measuring their effects on the 5-azacytidine-induced differentiation of C3H/10T1/2 cells because of inconsistencies in results. Mutagenic and oncogenic transformation in these cells is described. Mutagenesis data can be interpreted in various ways in order to obtain the desired result. In this system mutagenesis appears to be necessary but is not sufficient for transformation. (60 Refs)

# ENVIRONMENTAL RADIATION AND PROTECTION STANDARDS

## 25. REPORT OF AD HOC TASK FORCE ON INDOOR AIR POLLUTION.

**Dudney CS, Walsh PJ**
**Oak Ridge Natl. Lab., Oak Ridge, TN**
**Report of Ad Hoc Task Force on Indoor Air Pollution. Available from National Technical Information Service, Springfield, VA, as ORNL/TM-7679:, 245 pp., 1981.**

The quality of air within a man-made structure is likely to be affected by energy conserving modifications made on that structure. Information was reviewed on indoor air pollution and the potential impact on human health of energy conservation measures, primarily those to be applied in residences. Studies that have been done and those in progress indicate that indoor air pollution may significantly affect human health. The task force concluded from its investigations that (1) the indoor environment is likel y to include exposure to radon daughter nuclides, formaldehyde, carbon monoxide, nitrogen dioxide, respirable particulates, and asbestos, as well as other undefined pollutants; (2) indoor exposure may constitute 80 to 95% of the total exposure for some pollutants; (3) studies have not been done which provide a basis for an adequate assessment of indoor air quality; (4) some energy conservation measures reduce the rate of exchange between indoor and outdoor air; (5) reduced air exchange can lead to increased indoor levels of some pollutants; (6) increased indoor pollutant levels lead to increased exposure and increased risk of health impact; and (7) many federal agencies have an interest in various facets of indoor air pollution, but no agency has authority over the entire problem, and there has not been adequate coordination among the interested agencies. In light of the above, the task force recommends that a national policy on indoor air quality be developed and promulgated, the federal authority for establishment of indoor air quality guidelines and recommendations be clarified, and a lead agency be identified to develop a coordinated plan for studies of indoor air pollution with sufficient resources for its implementation. (Author abstract)

## 26. ESTIMATES OF INTERNAL DOSE EQUIVALENT TO 22 TARGET ORGANS FOR RADIONUCLIDES OCCURRING IN ROUTINE RELEASES FROM NUCLEAR FUEL-CYCLE FACILITIES, VOLUME III.

**Dunning DE, Killough GG, Bernard SR, Pleasant JC, Walsh PJ**
**Oak Ridge Natl. Lab., Oak Ridge, TN**
**Estimates of Internal Dose Equivalent to 22 Target Organs for Radionuclides Occurring in Routine Releases from Nuclear Fuel-Cycle Facilities, Volume III. Available from National Technical Information Service, Springfield, VA, as NUREG/CR-0150-V3:, 90 pp., 1981.**

This report is the third of a three-volume tabulation of internal radiation dose conversion factors for man for radionuclides of interest in environmental assessments of nuclear fuel cycles. This volume provides an updated summary of estimates of committed dose equivalent for 142 radionuclides considered in the previous two reports. Intakes by inhalation and ingestion are considered. The International Commission on Radiological Protection (ICRP) Task Group Lung Model has been used to simulate the deposition and retention of particulate matter in the respiratory tract. Results corresponding to activity median aerodynamic diameters (AMAD) of 0.3, 1.0, and 5.0 micrometers are given. The gastrointestinal (GI) tract has been represented by a four-segment catenary model with exponential transfer of radioactivity from one segment to the next. Retention of radionuclides in systemic organs is characterized by linear combinations of decaying exponential functions. Fifty-yr dose commitment per microcurie intake of each parent nuclide is given for 22 target organs including contributions from specified source organs plus the systemic activity residing in the rest of the body, cross irradiation due to penetrating radiations has been incorporated into these estimates. A separate tabulation of effective dose equivalent for all 142 radionuclides is provided also; this quantity, as defined by ICRP Publication 26, provides an indication of the overall health risk resulting from a radionuclide exposure. (Author abstract)

## 27. THE USE OF FILTERS TO REDUCE THE POTENTIAL ALPHA-ENERGY DUE TO RADON DAUGHTERS IN THE CABS OF MINING VEHICLES.

**Zettwoog P, Duport P, Campbell FE, Caplan HS**

**Commissariat a l'Energie Atomique, B.P. No 6, 9226 Fontenay-aux-Roses, France**

**Health Phys; 42(1):85-89 1982**

A theoretical analysis of the performance of filters for use in ventilation systems is presented. Filters were tested in a uranium mine to determine their effectiveness in reducing potential alpha-energy due to radon daughters in the cabs of mining vehicles. The filters were chosen based on their ability to withstand stringent conditions of shock and vibration. The Liebherr filter reduced the working level of alpha-energy in the machine cab by a factor of two. The filters also reduce ore dust levels. (7 Refs)

## 28. MEAN RESIDENCE TIME OF PLUTONIUM IN THE TROPOSPHERE.

**Holloway RW, Hayes DW**

**Environmental Protection Agency, P.O. Box 15027, Las Vegas, NV, 89114**

**Environ Sci Technol; 16(2):127-129 1982**

Natural radioactive tracers were used to estimate the mean residence time of plutonium in the troposphere. The results were then compared with those obtained using other methods. Residence time calculations were made for the yr 1971, 1974 and 1975. A June 1974 thermonuclear test by China injected debris into the stratosphere, while very little was detected in the troposphere during the summer and fall of 1974. Thus, 1974 was used for residence time calculations derived from the rate of decrease of the tropospheric air concentrations during the summer and fall mo. At six locations in the northern hemisphere the concentration of 239,240 Pu was calculated by converting the biomonthly concentrations for May through October to natural log form, and fitting a line to the three points by the least squares method. The av of the three residence times was 71 days; higher than most previous calculations of residence time (30-40 days), but in good agreement with results obtained using the 210Po/210Pb ratio (65 days). Since the 71-day residence time obtained was derived from particles that had been transported downward from the stratosphere to near the earth's surface, it is understandable that this value is much higher than some other methods using particles with very different origins. At widely dispersed locations in the northern hemisphere only slight variations of the mean residence time was observed. It is possible that the 71-day residence time estimated for plutonium-bearing particles is valid for natural aerosols in general. (17 Refs)

### 29. RESULTS OF ENVIRONMENTAL RADIOACTIVITY MEASUREMENTS IN THE MEMBER STATES OF THE EUROPEAN COMMUNITY FOR AIR, DEPOSITION, WATER, MILK IN 1979. RADIOLOGICAL PROTECTION NO. 20.

**Commission of the European Communities**

**Commission of the European Communities, Luxembourg, Luxembourg**

**Results of Environmental Radioactivity Measurements in the Member States of the European Community for Air, Deposition, Water, Milk in 1979. Radiological Protection No. 20. Available from National Technical Information Service, Springfield, VA, as PB82-123316:, 263 pp., 1981.**

This 19th report on environmental radioactivity, published by the Health and Safety Directorate of the Commission of the European Communities, is based on measurements of the radioactive contamination of the air, of deposition, of surface water, and of milk in each of the nine Member States during 1979. The results are presented under four main headings: (1) Artificial radioactivity in the air at ground level; (2) artificial radioactivity of deposition, ie fall-out and rain; (3) radioactivity of drinking water, surface waters, and the sea; and (4) radioactivity of milk. Measurements were made of specific nuclides and of overall radioactivity. A list of measuring laboratories and sampling stations for air, deposition, and milk is included, together with lists of available reports in this field published by the various Member States, by the JRC-Ispra, and the CEC. (Author abstract)

### 30. RADIATION DOSE ESTIMATES AND HAZARD EVALUATIONS FOR INHALED AIRBORNE RADIONUCLIDES.

**Mewhinney JA**

**Inhalation Toxicology Res. Inst., Lovelace Biomedical and Environmental Res. Inst., Albuquerque, NM**

**Radiation Dose Estimates and Hazard Evaluations for Inhaled Airborne Radionuclides. Available from National Technical Information Service, Springfield, VA, as NUREG/CR-2246:, 75 pp., 1981.**

The objective of this project is to conduct confirmatory research on the aerosol characterization, radiation dose distribution in animals following inhalation and to provide prediction of health consequences in humans due to airborne radioactivity which may be released in normal operations or under accident conditions during production of nuclear fuel composed of mixed oxides of U and Pu. Seven research reports are presented which summarize the results of specific areas of research being conducted. Two papers report on a series of in vitro dissolution studies conducted on aerosols containing uranium alone in several chemical forms and on an aerosol of U, Pu oxides involved in an accidental human exposure. Three papers report the results from studies in which rats, dogs and monkeys received inhalation exposure to aerosols of mixed U, Pu oxide or 'pure' PuO2. One paper presents a detailed accounting of the mathematical and statistical procedures developed to conduct health risk estimates for humans from the research results in animals and one paper presents the statistical basis for the design of the study designed to determine the relationship of radiation dose to biological effect in rats following inhalation of aerosols formed in mixed oxide fuel fabrication. (Author abstract)

### 31. DARTAB: A PROGRAM TO COMBINE AIRBORNE RADIONUCLIDE ENVIRONMENTAL EXPOSURE DATA WITH DOSIMETRIC AND HEALTH EFFECTS DATA TO GENERATE TABULATIONS OF PREDICTED HEALTH IMPACTS.

**Begovich CL, Eckerman KF, Schlatter EC, Ohr SY, Chester RO**
**Oak Ridge Natl. Lab., Oak Ridge, TN**
**DARTAB: A Program to Combine Airborne Radionuclide Environmental Exposure Data with Dosimetric and Health Effects Data to Generate Tabulations of Predicted Health Impacts. Available from National Technical Information Service, Springfield, VA, as DE81030434:, 79 pp., 1981.**

The DARTAB computer code combines radionuclide environmental exposure data with dosimetric and health effects data to generate tabulations of the predicted impact of radioactive airborne effluents. DARTAB is independent of the environmental transport code used to generate the environmental exposure data and the codes used to produce the dosimetric and health effects data. Therefore human dose and risk calculations need not be added to every environmental transport code. Options are included in DARTAB to permit the user to request tabulations by various topics (eg, cancer site, exposure pathway, etc) to facilitate characterization of the human health impacts of the effluents. The DARTAB code was written at ORNL for the US Environmental Protection Agency, Office of Radiation Programs. (Author abstract)

### 32. ROUTINE PREVENTION OF ABUSIVE IRRADIATION IN NUCLEAR MEDICINE.

**Ducassou D**
**Service de Medecine Nucleaire, Hopital du Haut-Leveque, F 33604 Bordeaux-Pessac, France**
**J Radiol; 62(11):596-597 1981**

When using radionuclide scanning the advantages and risk associated with the technic must be balanced. Radiation doses delivered to the target organ during scintigraphic examination of the liver, lungs, bone, and spleen are described. Minimization of dose, protection of personnel and of workers who produce the radiopharmaceuticals are discussed. The role of the doctor in preventing abuse of radiodiagnostics is considered. (6 Refs) (In FRE)

## REVIEWS AND OTHER STUDIES

### 33. RADIOSENSITIVITY VARIATION DURING THE CELL CYCLE IN PRONUCLEAR MOUSE EMBRYOS IN VITRO.

**Domon M**
**Dept. Dental Radiology, Tokyo Medical and Dental Univ., 1-5-45 Yushima, Bunkyo-ku, Tokyo, Japan**
**Cell Tissue Kinet; 15(1):89-98 1982**

The radiosensitivity of pronuclear mouse (B6D2 F1 x ICR) embryos has been measured in vitro as a function of time during the cell cycle. This was done by measuring the dose of x-rays (LD50) required to prevent development of 50% of the pronuclear embryos to the blastocyst stage in 5 days of culture. The LD50 was found to vary from 1 to 2 Gy during the period from G1 to the first cleavage. The cell cycle in the pronuclear embryo was analyzed by [3H]thymidine autoradiography. Compared with earlier studies on two-cell mouse embryo radiosensitivity, the pronuclear embryos appear to be more sensitive to radiation than the two-cell embryos. If, however, one considers the radiation sensitivity on a blastomere basis, the pronuclear embryos are not different in their radiation sensitivity from the two-cell embryos. Thus, during the early cleavage stages of mice, radiosensitivity is mainly governed by the content of cells of various cell cycle ages in the embryo. (Author abstract) (33 Refs)

### 34. THE BIOLOGICAL EFFECTS OF LOW-LEVEL IONIZING RADIATION.

**Upton AC**
**Inst. Environmental Medicine, New York Univ. Sch Medicine, New York, NY**
**Sci Am; 246(2):41-49 1982**

The biological hazard resulting from exposure to low-level ionizing radiation (IR) is discussed. IR occurs as electromagnetic or particulate radiation and may have a low or high rate of linear energy transfer (LET). IR may produce early transitory effects and/or late carcinogenic or heritable effects. Occurrence of nonheritable effects is apparently dose-rate-related and displays a threshold effect. Heritable effects apparently increase with total dose and display no threshold effect. Low-LET IR is more likely to produce simple forms of DNA damage that are likely to be repaired by cellular mechanisms when the IR dose rate is low. High-LET IR is more likely to produce more serious DNA damage that is more likely to be incorrectly repaired or remain unrepaired. Analysis of studies in animals and in three groups of humans (survivors of atomic bombings, patients undergoing radiological medical procedures, and those receiving occupational exposure to IR) shows an increase in breast cancer and leukemia with total exposure to IR. No heritable genetic damage has been demonstrated among children of atomic bomb survivors. Current data indicates that naturally occurring background IR accounts for 1-3% of all cancer fatalities, and that risks resulting from occupational exposure are small compared with other risks in daily life. (no Refs)

### 35. PITUITARY AND STEROID HORMONES IN RADIATION-INDUCED MAMMARY TUMORS.

**Shellabarger CJ**
**Medical Dept., Brookhaven National Lab., Upton, NY, 11973**
**Banbury Rep; 8:339-351 1981**

Advantages of the radiation-induced (RI) rat mammary tumor system as a mode for studying RI breast cancer in humans and the rat mammary fibroadenoma response to irradiation are discussed. Evidence for chemically induced carcinogenesis and RI carcinogenesis is compared. Estrogen synergism in mammary carcinogenesis is reviewed; women whose cancer is 'initiated' women may develop breast cancer if the disease is 'promoted,' even if the promotion occurs years after initiation. (57 Refs)

### 36. URANIUM MINER LUNG CANCER STUDY. PROGRESS REPORT, 1 JULY 1980-1 JULY 1981.

**Saccomanno G**
**Saint Mary's Hosp. and Medical Center, Grand Junction, CO**
**Uranium Miner Lung Cancer Study. Progress Report, 1 July 1980 - 1 July 1981. Available from National Technical Information Service, Springfield, VA, as DE81030162:, 8 pp., 1981.**

The projects supported during the past year consist of: (a) collection of material from uranium miners known to have cancer of the lung into a tumor registry; (b) collection of interesting cases for second edition of the Manual on Pulmonary Cytology; (c) the regression study has been modified by computerization of rereads of all cases which showed moderate atypical squamous cell metaplasia or higher since 1968; (d) continuation of sputum collection, and collection of lungs from decreased miners; (e) cooperation with fluorescent bronchoscopy development for localization of carcinoma in situ of the lung; (f) the immunological studies are presently funded by the Abbott Laboratories, but are closely associated with the lung cancer studies. Our findings suggest that patients developing lung cancer concomitantly develop immune suppression; and (g) a small plastic tube has been developed which will aid in the removal of cells from fiberoptic brushings. The plastic mold is presently being developed by Midi-Tech Corporation in Boston and the tube will be available in September 1981. Analysis of the incidence of small cell cancers of the lung over the last 30 yr indicates that the incidence has dropped to 22% during 1975-1979 whereas it was 76.5% during the 5 yr span from 1954-1959. General observations indicate that cigarette smoking is the most potent carcinogen, but that tumors are increased in miners who smoke. Moreover, the ultimate incidence of oat cell carcinoma results in earlier death than with other tumor types. The most commonly found tumor in the non-smoking miner is the small cell type. (Author abstract)

### 37. MALIGNANT PULMONARY NEOPLASM AND INHALANT RADIATION EXPOSURE.

**Seve J**
**Centrum hygieny zareni, Institut hygieny a epidemiologie, Srobarova 48, 100 42 Prague 10, Czechoslovakia**
**Cas Lek Cesk; 120(48):1440-1441 1981**

Long-term cohort studies on the relationship between occupational exposure to inhaled radioactive substances and malignant pulmonary neoplasms in miners in Czechoslovakia, USA and Sweden are reviewed. The results concurrently confirmed lung tumor incidence in miners to be dependent on accumulated exposure to radon daughters, and alike elements, age at the onset of exposure, annual radiation do se and cigarette smoking. No specific histological type, and no increased mortality due to other malignant tumors were found. (17 Refs) (In CZE)

### 38. ATOMIC BOMBS AND GENETIC DAMAGE.

**Berry RJ**
**Dept. Zoology, Univ. Coll. London, London WC1E 6BT, England**
**Br Med J; 284(6313):366-367 1982**

Human resistance to genetic damage from radiation is discussed. Studies of individuals exposed to atomic radiation at Hiroshima and Nagasaki fail to identify any significant mutational effects of radiation. Relationships between genetic damage and radiation dose are considered in both humans and animals. (13 Refs)

### 39. RECENT ADVANCES IN CANCER CYTOGENETICS.

**Pogosiants EE**
**All-Union Cancer Res. Center, Moscow, USSR**
**Genetika; 17(12):2087-2099 1981**

Recent studies in the field of cancer cytogenetics are reviewed with special emphasis on karyotypic changes in leukemia and carcinoma cells, prezygotic chromosome mutations specific for certain human tumors, and phenomena of gene amplification characteristic for a number of tumors and for cells resistant to antineoplastic agents. Specific karyotypic changes were observed in human and murine leukemias, as well as in a number of experimental sarcomas and carcinomas. Specific involvement of chromosome 15 was recorded in murine radiation-induced and carcinogen-induced T-cell leukemias; also, trisomy for chromosome 15 or translocation involving chromosome 15 were detected in B-cell leukemias and lymphomas. Specific involvement of the distal third of chromosome 15 indicated that this region contains the cluster of genes responsible for normal differentiation and malignant transformation of lymphoreticular cells. Specific prezygotic chromosome aberrations were observed in retinoblastoma (deletion in the long arm of chromosome 13), nephroblastoma (deletion in the short arm of chromosome 11), and in familial kidney carcinoma (translocation between chromosomes 3 and 8). Specific resistance of eukaryotic cells to methotrexate was shown to be associated with the presence of homogenously stained regions and the number of double microchromosomes. (73 Refs) (In RUS)

## 40. RADIATION RISKS IN INFANTS AND CHILDREN.

**Faure C**

**Service de Radiologie, Hopital Trousseau, 8 a 28 avenue du Dr. Arnold-Netter, F 75710 Paris Cedex 12, France**

**J Radiol; 62(11):566-567 1981**

Somatic and genetic risks associated with radiation of newborns, infants, and children are discussed. The association of thyroid cancer and low dose radiation of the thyroid during childhood for thyroid adenomas or hyperplasia and of breast cancer and childhood irradiation for scoliosis provides evidence for increased cancer risk among irradiated children. Childhood irradiation also has been related to an increased incidence of leukoses. The genetic risks of irradiation are similar in adults and children . Factors related to increased somatic risk in irradiated children are discussed. (11 Refs) (In FRE)

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Sram RJ, Tomatis L, Bridges BA, Clemmesen J
(c/o Lohman), Medical Biological Lab. TNO, P.O. Box 45, 2280 AA Rijswijk, The Netherlands
Mutat Res; 87(3):299-319 1981

2. ETHYLENE DIBROMIDE (EDB). (REVISED).
NIOSH Document Development Branch
Robert A. Taft Lab., National Inst. Occupational Safety and Health, 4676 Columbia Parkway, Cincinnati, OH, 45226
Curr Intell Bull NIOSH (37): 13 pp., 1981.

3. CHEMICAL CARCINOGENESIS AND SMOKING.
Farber E
Dept. Pathology, Univ. Toronto, Banting Inst., 100 College St., Toronto, Ontario M5G 1L5, Canada
Can J Public Health; 72(6):381-385 1981

## RADIATION CARCINOGENESIS

4. CELLULAR TRANSFORMATION BY RADIATION: INDUCTION, PROMOTION, AND INHIBITION.
Borek C
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J Supramol Struct Cell Biochem; 16(4):311-336 1981

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## DIETARY FACTORS IN CARCINOGENESIS

6. BETA-CARBOLINES, PSYCHOACTIVE COMPOUNDS IN THE MAMMALIAN BODY.
Airaksinen MM, Kari I
Dept. Pharmacology, Univ. Kuopio, P.O. Box 138, SF-70101 Kuopio 10, Finland
Med Biol; 59(4):190-211 1981

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Zaridze DG
Analytical Epidemiology Programme, Div. Epidemiology and Biostatistics, International Agency for Res. on Cancer, 150 Cours Albert Thomas, 69372 Lyon, Cedex 2, France
Nutr Cancer; 2(4):241-249 1981

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Dept. Physiological Nursing, Sch. Nursing, Univ. Washington, Seattle, WA
Cancer Nursing. Marino LB, ed. St. Louis, The C. V. Mosby Company, 635 pp., 1981.

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Balda BR
Dermatologische Klinik und Poliklinik der Universitat, Frauenlobstr. 9-11, D-8000 Munchen 2, W. Germany
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Kaw JL
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Dept. Epidemiology and Biometry, Inst. Occupational Health, Haartmaninkatu 1, SF-00290 Helsinki 29, Finland
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15. ALKYLATION OF DNA AND TISSUE SPECIFICITY IN NITROSAMINE CARCINOGENESIS.
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Lab. Molecular Virology, NCI, Frederick, MD, 21701
Adv Cancer Res; 35:27-47 1981

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Koyama T
Dept. Carcinostasis Res., Tokyo Univ. Medical Res. Inst., 4-6-1 Kindai, Minato-ku, Tokyo 108, Japan
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Eckhart W
Tumor Virology Lab., Salk Inst., San Diego, CA, 92138
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Office of Technology Assessment
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Assessment of Technologies for Determining Cancer Risks from the Environment. Available from National Technical Information Service, Springfield, VA, as PB81-235400:, 243 pp., 1981.

21. ANTIBODIES SPECIFIC FOR DNA COMPONENTS STRUCTURALLY MODIFIED BY CHEMICAL CARCINOGENS.
Muller R, Rajewsky MF
(c/o Rajewsky) Institut fur Zellbiologie (Tumorforschung), Universitat Essen (GH), Hufelandstrasse 55, Essen 1, W. Germany
J Cancer Res Clin Oncol; 102(2):99-113 1981

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Takemura N
Dept. Public Health, Jikei Univ., 25-8, Nishi-Shimbashi 2-chome, Minato-ku, Tokyo, 105, Japan
Sangyo Igaku; 23(4):355-365 1981
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## OTHER REVIEWS IN CARCINOGENESIS

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Levine L
Dept. Biochemistry, Brandeis Univ., Waltham, MA, 02254
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Scalabrino G, Ferioli ME
Inst. General Pathology, Univ. Milan, 20133 Milan, Italy
Adv Cancer Res; 35:151-268 1981

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# RADIATION CARCINOGENESIS

SERIES CK06 No. 82/08

AUGUST, 1982

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## RADIATION CARCINOGENESIS IN HUMANS

### 1. EPIDEMIOLOGIC CHARACTERISTICS OF CHILDHOOD CANCER.

**Austin DF, Nelson VE, Johnson LF**
**Resource for Cancer Epidemiology, Health Services, 1450 Broadway, Oakland, CA, 94612**
**Front Radiat Ther Oncol; 16:9-17 1982**

In the San Francisco metropolitan area, the incidence of malignancies in childhood (0-19 yr old) remained substantially unchanged over a 10-yr period (1969-1978), but the mortality rate

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declined substantially in all pediatric age groups. The mortality/incidence ratio in all age groups combined declined by about 20% during this time, apparently reflecting improved treatment procedures. These changes have been greater in children 0-14 yr old than in the 15-19 age group. Examination of mean annual age-specific mortality rates for the leukemias suggests that leukemias (especially acute leukemias) of childhood and adulthood may be etiologically different diseases. There responses to treatment suggest that they may be biologically different diseases. Possible etiologic factors for childhood leukemia include prenatal radiation exposure, chromosomal abnormalities, and possibly antigenic stimulation of the WBC population at a critical period of gestation by certain biologic agents. The children of women who had been in the first trimester of pregnancy during an influenza A epidemic showed a 3-4-fold increase in the risk of childhood leukemia. Investigations of childhood leukemia clusters have almost uniformly been inconclusive. A cluster of Ewing's sarcoma (30 recorded cases over an 8-yr period; 20% of the entire 8-yr incidence) has been discovered in one small community (within a 30-block diameter) in the San Francisco area. It is hoped that investigations of such clusters may provide clues for the prevention of the disease. (6 Refs)

### 2. THE RISK OF SECOND PRIMARIES SUBSEQUENT TO IRRADIATION FOR CERVIX CANCER.

**Lee JY, Perez CA, Ettinger N, Fineberg BB**

**(c/o Perez) Div. Radiation Oncology, Mallinckrodt Inst. Radiology, Washington Univ. Sch. Medicine, 4511 Forest Park, St. Louis, MO, 63108**

**Int J Radiat Oncol Biol Phys; 8(2):207-211 1982**

The risk of developing a new primary malignancy following radiation therapy (RT), alone or combined with surgery, for invasive cancer of the uterine cervix was studied in 1,048 patients with histologically proven invasive carcinoma Stages I, II, or III, who were followed up with a median period of 4 yr. During the observation time 32 second primaries (SP) were reported. No statistically significant difference between the observed and expected number of SP was noted. Using the person yr approach, the SP incidence rate was 5.49/1,000 person-yr. Eleven SP were observed in the pelvic region: colon, rectum, endometrium, and vagina, while 20 occurred outside the pelvis. Neither the incidence of pelvic SP nor that of extra-pelvic SP was greater than expected. The time from RT to diagnosis of a SP ranged from 1 to 16 yr with a median of 8 yr for pelvic SP, and 6 yr for extra-pelvic SP. The incidence of SP increased with the stage of cervix cancer; the increase is statistically significant. Mean ages of Stage II and Stage III patients were higher than that of Stage I patients. No significant difference of a possible carcinogenic effect of RT was noted between the patients treated with RT alone (6,000-8,000 rad) and patients treated preoperatively or postoperatively (3,000-5,000 rad). SP had no impact on the survival experience of the study population in the first 5 yr after treatment; after 5 yr some deaths were observed, but patients are at higher risk of death from other causes than from SP. (15 Refs)

## EXPERIMENTAL RADIATION CARCINOGENESIS

### 3. MODULATION OF SURVIVAL AND TRANSFORMATION DURING PLATEAU-PHASE HOLDING OF UV-IRRADIATED MOUSE CELLS.

**Chan GL, Little JB**

**Sidney Farber Cancer Inst., 44 Binney St., Boston, MA, 02115**

**Mutat Res; 104(1-3):183-186 1982**

C3H 10T1/2 mouse fibroblasts were cultured for various time periods in the quiescent phase of growth following UV irradiation, to allow DNA repair to occur prior to the initiation of DNA replication. Biological effects of the repair processes were measured with respect to end points of clonogenic survival and malignant transformation. In the first hr of plateau-phase holding after 10 Joules/square meter of UV light, a 1.7-fold survival enhancement was observed, with most of the recovery occurring within the first 6 hr of holding. In experiments where fresh medium was given to 10T1/2 cells during the holding period, the survival enhancement was slightly more than two-fold. In the initial 6 hr of holding, an enhancement in the transformation frequency was observed. In the initial holding period, an error-prone mode of pyrimidine-dimer repair may give rise to both enhanced survival and transformation. The role of pyrimidine dimers in lethality and transformation in 10T1/2 cells is discussed. (17 Refs)

### 4. PROLIFERATIVE AND MORPHOLOGICAL CHANGES IN THE PULMONARY EPITHELIUM OF THE SYRIAN GOLDEN HAMSTER DURING CARCINOGENESIS INITIATED BY 210POALPHA ALPHA-RADIATION.

**Shami SG, Thibodeau LA, Kennedy AR, Little JB**

**Inhalation Toxicology Res. Inst., Lovelace Biomedical and Environmental Res. Inst., P.O. Box 5890n Ave., Albuquerque, NM, 87185**

**Cancer Res; 42(4):1405-1411 1982**

The role of cellular proliferation in a two-stage model of carcinogenesis in the hamster lung was investigated. Syrian golden hamsters were treated intratracheally with either one instillation of 0.2 uCi of 210Po (Po-O group), seven weekly instillations of BP (O-BP group), or 0.2 uCi 210Po followed 15 wk later by either seven instillations of 0.9% NaCl solution (Po-Sal group) or seven instillations of BP (Po-BP group). All BP instillations were 3 mg each of BP:ferric oxide (1:1, w/w) carrier particles. Serial sacrifices were performed for up to 85 wk. Two hr before sacrifice, each animal was given ip injections of 200 uCi of [3H]thymidine. Glycol methacrylate section autoradiographs (1 um) were prepared. Labeling indices in the alveolar region, labeling of terminal bronchiolar cells, and morphological changes were examined. Equal numbers of Po-Sal and Po-BP animals developed lung tumors. No tumors were found in Po-O or O-BP animals. Tumor development was preceded by the appearance of hyperplastic areas of bronchiolar-type cells in the alveolar region and by changes in morphology of bronchiolar cells. Labeling indices in the alveolar region of the treated groups were slightly increased relative to untreated controls. Labeling of terminal bronchiolar cells was highest in the Po-BP and O-BP groups and was associated with much inflammation. A single 0.9% NaCl solution instillation also increased proliferation of bronchiolar cells. We conclude that 0.9% NaCl solution instillations may potentiate carcinogenesis in the hamster lung by acting as a nonspecific stimulus to proliferation; in addition, we conclude that not all hyperplasia progressed on to form lung tumors in the Po-BP and Po-Sal groups. (Author abstract) (50 Refs)

### 5. DETECTION OF DUCTAL DYSPLASIA IN MAMMARY OUTGROWTHS DERIVED FROM CARCINOGEN-TREATED VIRGIN FEMALE BALB/C MICE.

**Ethier SP, Ullrich RL**
**Biology Div., Univ. Tennessee-Oak Ridge Graduate Sch. Biomedical Sciences, Oak Ridge, TN, 37830**
**Cancer Res; 42(5):1753-1760 1982**

These studies were undertaken to determine if altered growth potential of mammary epithelial cells could be detected in outgrowths derived from monodispersed mammary cells of virgin female BALB/c mice previously exposed to ionizing radiation or 7,12-dimethylbenz(a)anthracene (DMBA). Monodispersed mammary epithelial cells were obtained by enzymatic dissociation of mammary tissues of 12-wk-old virgin female BALB/c mice. Twenty-four hr prior to cell dissociation, donor animals were exposed to either 100 rads of gamma-ray irradiation, 0.25 mg of DMBA, or 0.075 mg of DMBA. Control donors were untreated. Mammary outgrowths were derived by injecting cells into the gland-free mammary fat pads of 3-wk-old virgin female BALB/c mice. Ten wk after the injection, the outgrowths were examined and classified. The data indicated that treatment of donor animals with either gamma-radiation or DMBA increased the frequency of ductal lesions over control levels. Both the frequency and severity of the lesions depended on the number of cells which were injected. When outgrowths were derived by injection of 10(5) cells into the gland-free fat pads, only a few severe lesions were detected. In outgrowths derived from 10(4) cells, less severe lesions (Class I lesions) were common in all groups and occurred in approximately 10 to 15% of the outgrowths. The frequency of severe (Class II and III) ductal dysplasia, however, was increased by treatment in these groups, occurring in 4.5% of control outgrowths in 15.6, 14.9, and 14.3% of the outgrowths derived from donor cells treated with 100 rads gamma-rays, 0.075 mg DMBA, and 0.25 mg DMBA, respectively. Thus, these data indicated that ductal dysplasias were more common and more severe in outgrowths derived from 10(4) rather than 10(5) cells. The ductal lesions observed in this study resembled both morphologically and histologically ductal abnormalities which have been associated with the pathogenesis of mammary carcinoma in both rats and mice. (29 Refs)

### 6. CAUSES OF DEATH AND THEIR CONTRIBUTION TO RADIATION-INDUCED LIFE SHORTENING IN INTACT AND OVARIECTOMIZED MICE.

**Storer JB, Mitchell TJ, Ullrich RL**
**Biology Div., Oak Ridge Natl. Lab., Oak Ridge, TN, 37830**
**Radiat Res; 89(3):618-643 1982**

Both intact and ovariectomized RFM and BALB/c mice were given multiple dose levels of gamma radiation (137Cs, 40 rad/min) to examine the role of the ovary in life shortening, with emphasis on possible changes in the incidence of neoplasms. Radiation-induced life shortening was significantly greater in intact vs ovariectomized mice. Life shortening injury in intact animals exhibited both a dose-dependent and a dose-independent component, with ovariectomy abolishing the dose-independent component. Classification of tumors on the basis of lethality and prevalence permitted calculation of the relative death risk as a function of dose for each disease category. In intact mice the dose-independent life shortening was due solely to nonneoplastic causes. The dose-dependent component of life shortening was due entirely to lethal neoplasms in both strains. For BALB/c mice lethal solid tumors and reticular tissue tumors were the major cause of death, while in the RFM strain reticular tissue tumors predominated. Ovariectomy in both strains reduced radiation-induced neoplasms. Host factors apparently play a major role in tumor expression and radiation-induced life shortening in mice is primarily due to neoplastic causes. (22 Refs)

### 7. SYSTEMIC INFLUENCE OF PRE-IRRADIATION OF A LIMITED SKIN AREA ON UV-TUMORIGENESIS.

**de Gruijl FR, Van der Leun JC**
**Inst. Dermatology, State Univ. Utrecht, Utrecht, The Netherlands**
**Photochem Photobiol; 35(3):379-383 1982**

It has been established that chronic UV irradiation of mice produces a systemic effect. The animals become incapable of rejecting an implanted UV-induced tumor. A possible consequence of the induction of this systemic effect could be an enhancement of the de novo formation of tumors by chronic UV irradiation. We have therefore carried out an investigation to determine whether such an effect is demonstrable in an animal model. Hairless mice (Skh hr 1) were pre-irradiated for a few mo with UV radiation while certain skin areas of the animals were shielded from the radiation. Subsequently, the initially shielded skin areas were chronically exposed to UV radiation, which resulted in the development of tumors in these skin areas. It was found that the formation of tumors in the initially shielded skin areas was enhanced by the pre-irradiation of the other skin areas. Thus, a systemic effect appeared to have influenced the development of tumors in the initially shielded skin areas. (Author abstract) (12 Refs)

### 8. RETINOIC ACID MODULATION OF ULTRAVIOLET LIGHT-INDUCED EPIDERMAL ORNITHINE DECARB OXYLASE ACTIVITY.

**Lowe NJ, Breeding J**
**Div. Dermatology, Univ. California Los Angeles Sch. Medicine, Los Angeles, CA, 90024**
**J Invest Dermatol; 78(2):121-124 1982**

Irradiation of skin with UV light of sunburn range (UVB) leads to a large and rapid induction of the polyamine biosynthetic enzyme ornithine decarboxylase in the epidermis. Induction of epidermal ornithine decarboxylase also occurs following application of the tumor promoting agent 12-O-tetradecanoylphorbol-13 acetate and topical retinoic acid is able to block both this ornithine decarboxylase induction and skin tumor promotion. In the studies described below, topical application of retinoic acid to hairless mouse skin leads to a significant inhibition of UVB-induced epidermal ornithine decarboxylase activity. The degree of this inhibition was dependent on the dose, timing, and frequency of the application of retinoic acid. To show significant inhibition of UVB-induced ornithine decarboxylase the retinoic acid had to be applied within 5 hr of UVB irradiation. If retinoic acid treatment was delayed beyond 7 hr following UVB, then no inhibition of UVB-induced ornithine decarboxylase was observed. The quantities of retinoic acid used (1.7 nmol and 3.4 nmol) have been shown effective in inhibiting 12-O-tetradecanoyl phorbol-13 acetate induced ornithine decarboxylase. The results show that these concentrations of topical retinoic acid applied either before or immediately following UVB irradiation reduces the UVB induction of epidermal ornithine decarboxylase. The effect of retinoic acid in these regimens on UVB-induced skin carcinogenesis is currently under study. (Author abstract) (20 Refs)

## EXPERIMENTAL RADIATION MUTAGENESIS

### 9. MUTATIONS INDUCED BY X-RAYS AND UV RADIATION DURING THE NUCLEAR CELL CYCLE IN THE YEAST SCHIZOSACCHAROMYCES POMBE.

**Barale R, Rusciano D, Loprieno N**
**Istituto di Biochimica, Biofisica e Genetica, Univ. Pisa, Pisa, Italy**
**Mutat Res; 92(1/2):39-47 1982**

A cell division cycle (CDC) mutant of Schizosaccharomyces pombe ade 6-60, we 1-50 was used to produce a large population of cells synchronized in nuclear stage G1. The cells were exposed to different doses of UV or x-rays at various times during the progression from G1 to nuclear stage G2. The CDC stages showing the highest sensitivity to the lethal and mutagenic effects of both types of radiation were the DNA prereplicative and replicative phases. The induction of mutations seemed to depend on the number of unrepaired DNA lesions reaching the replicating fork or occurring at that time. The x-ray-induced mutations were saturated earlier than the UV-induced mutations, perhaps because x-rays induced a larger amount of lethal damage. (13 Refs)

### 10. THE MUTAGENIC EFFECTS OF DIEPOXYBUTANE IN WILD-TYPE AND MUTAGEN-SENSITIVE MUTANTS OF DROSOPHILA MELANOGASTER.

**Olsen OA, Green MM**
**Inst. General Genetics, Univ. Oslo, P.O. Box 1031 Blindern, Oslo 3, Norway**
**Mutat Res; 92(1/2):107-115 1982**

The effects of 1,2,3,4-diepoxybutane (DEB) on two X-chromosome loci (w and y) of Drosophila were studied. At least one-third of the DEB-induced mutations were chromosome deletions. The nature of the DEB-induced complementary mutants was not clear. Some of the mutants were mosaics, expressed somatically but not transmitted in the germ line. Somatic sensitivity to DEB was demonstrated by 9/11 methyl methanesulfonate (MMS)-sensitive mutants. The MMS-sensitive and DEB-insensitive mutants were also somatically insensitive to nitrogen mustard and UV (one was also insensitive to x-rays), suggesting that these mutants (mus103 and mus105) may not be involved in DNA replication or repair. In direct genetic experiments, females homozygous for at least 2/6 and probably 5/6 MMS-sensitive mutants showed an impaired capacity to repair DEB-induced damage in spermatozoa. Females homozygous for MMS-sensitive mutant mus201 showed an unimpaired capacity to repair DEB-induced genetic damage. (15 Refs)

## EFFECTS OF IRRADIATION ON CHROMOSOMES AND DNA

### 11. ABNORMAL LEVELS OF UV-INDUCED UNSCHEDULED DNA SYNTHESIS IN ATAXIA TELANGIECTASIA CELLS AFTER EXPOSURE TO IONIZING RADIATION.

**Jaspers NG, Bootsma D**
**Lab. Cell Biology and Genetics, Erasmus Univ. Rotterdam, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands**
**Mutat Res; 92(1/2):439-446 1982**

The baseline levels of UV-induced unscheduled DNA synthesis (UDS) in normal human fibroblast cell lines (C3RO and C5R0) and ataxia-telangiectasia (AT) fibroblast cell lines (AT5BI, AT4BI, AT2BE, AT1PWA, and AT3BI) were determined to be the same. Exposure to x-rays (XR: up to 20,000 rads) significantly altered UV-induced UDS in the AT cells but not in the normal cells. In AT cell lines showing a reduced capacity for gamma-ray-induced repair DNA synthesis (excision-deficient AT cell lines AT3BI and AT2BE), XR exposure inhibited UV-induced UDS. In AT cell lines showing a normal capacity for gamma-ray-induced repair DNA synthesis (excision-proficient AT cell lines), XR exposure stimulated UV-induced UDS. The excision-deficient and excision-proficient AT cell lines showed different dose-response relationships for both UV and XR. The two types of AT cells may have different molecular defects. Altered levels of repair DNA synthesis after UV exposure in AT cells may be secondary consequences of the way the cells handle DNA damage induced by ionizing radiation. (14 Refs)

### 12. A SYSTEM FOR MEASURING THE FREQUENCIES OF TANDEM AND NON-TANDEM DOUBLE BASE SUBSTITUTIONS INDUCED BY ULTRAVIOLET IRRADIATION.

**Dunst RW, Coleman RD, Harnish BW, Hill CW**
**(c/o Hill) Dept. Biological Chemistry, Specialized Cancer Res. Center, Milton S. Hershey Medical Center, Pennsylvania State Univ., Hershey, PA, 17033**
**MGG; 184(3):445-449 1981**

A system based on missense suppressor mutations affecting an Escherichia coli glycine tRNA was used for measuring the relative frequencies of a single base substitution, a tandem double base substitution and a non-tandem double base substitution all occurring in the same triplet and in the same mutagenic treatment. RNA sequencing studies reported here have shown that the glyUsuGAA mutation results from a CCC-TTC tandem double substitution in the anticodon region of the gene coding for tRNAGly/GGG. Following mutagenesis the culture is induced for phage production and the resulting lysate assayed for phage carrying any one of the three suppressor alleles. An important feature of the system is that it circumvents the problem of distinguishing the rare double mutations from the more abundant background. We have found that with doses of UV irradiation sufficient to reduce the viable cell count 98-99%, the tandem double base substitution occurs 0.01 as frequently as the single. The tandem double substitution occurs about 4x more frequently than the nontandem double substitution. The sequence studies utilized a recombinant plasmid bearing the glyUsuGAA allele inserted between the EcoRI and SalI sites of pBR313 as well as defective lambda transducing phage in order to amplify and selectively label the suppressor tRNA. Thus the mutant tRNA could be purified sufficiently to permit sequencing despite the fact that it is aminoacylated very poorly. It was found that the nature and extent of tRNA modification varied with the method of amplification. Namely, use of the plasmid for amplification resulted in variable levels of 2'-O-methyl-G at position 17, while use of the phage resulted in variable modification of a G in the anticodon stem. (12 Refs)

### 13. 12-O-TETRADECANOYL-PHORBOL-13-ACETATE AND ITS RELATIONSHIP TO SCE INDUCTION IN SYRIAN AND CHINESE HAMSTER CELLS.

**Popescu NC, Amsbaugh SC, Larramendy ML, DiPaolo JA**
**Lab. Biology, Building 37, Room 2A19, NCI, Bethesda, MD, 20205**
**Environ Mutagen; 4(1):73-81 1982**

Alteration of cell culture conditions, 12-O-tetradecanoylphorbol-13-acetate (TPA), or 5-bromodeoxyuridine (Burd) concentrations, or temporal relation between UV or x-irradiation and TPA had no effect on sister chromatid exchange (SCE) induction of Syrian hamster embryo cells (HEC). SCE frequencies were determined on exponentially growing and stationary HEC cultures incubated with different Burd concentrations for one or two replicative cycles. TPA (0.01-2.0 ug/ml medium) was ineffective in inducing SCE in HEC cultures cultivated in medium supplemented with heat-inactivated serum, independent of Burd concentration (1.0-10.0 ug/ml) and the number of cell divisions post treatment. In a similar study, TPA did not increase SCE frequency in V79-4 Chinese hamster cells in heat-inactivated or noninactivated serum. TPA has no effect on UV or x-irradiation induced SCE. X-irradiation (200 R) causes an increase of only 1 SCE/cell over the control value, while UV (1.5 and 3.0 J/square meter) causes an increase of 10 and 24 SCE per metaphase. TPA addition either immediately or 48 hr after UV or x-irradiation did not alter SCE frequency obtained by irradiation alone. Although SCE induction may be important for the induction of transformation by environmental agents, the enhancement of transformation frequency caused by TPA occurs without further DNA alterations involved in SCE formation. (21 Refs)

### 14. 12-O-TETRADECANOYLPHORBOL-13-ACETATE (TPA) INDUCES SISTER-CHROMATID EXCHANGES AND DELAYS IN CELL PROGRESSION IN CHINESE HAMSTER OVARY AND HUMAN CELL LINES.

**Schwartz JL, Banda MJ, Wolff S**
**Lab. Radiobiology, Univ. California, San Francisco, CA, 94143**
**Mutat Res; 92(1/2):393-409 1982**

In Chinese hamster ovary (CHO) cells and SV40-transformed human fibroblast cell lines (GM637 and XP12RO), 12-O-tetradecanoylphorbol-13-acetate (TPA: 1.0 nanog-1.0 ug/ml) caused a 20-45% increase in the frequency of sister chromatid exchanges (SCEs). This increase in SCEs was not caused by an impurity in the TPA preparation, or increased 5-bromo-2'-deoxyuridine uptake into DNA; it was independent of the incubation time between TPA exposure and fixation of the cells. Simultaneous exposure to TPA (1.0 ug/ml) and benzo(a)pyrene (BP: 1.7 x 10(-5)-3.3 x 10(-6) M) led to a synergistic SCE induction in CHO cells. No synergism was observed after simultaneous exposure to TPA (1 ug/ml) and mitomycin C (0.03 ug/ml) or UV light. In addition to its weak SCE-inducing effects in CHO cells, TPA alone caused a slight delay in cell cycle progression and markedly enhanced the cell cycle delay induced by BP. The SCE-inducing capacity of TPA in these cells was unrelated to its toxicity, because TPA was not toxic at the doses used. It also seemed to be unrelated to excision repair capacity, because TPA caused similar increases in SCE frequency in cells which were proficient (GM637), mildly deficient (CHO), and severely deficient (XP12RO) in excision repair. The significance of SCE induction and its relationship to other biologic effects of TPA remain unknown. (40 Refs)

### 15. DIFFERENTIAL PERSISTENCE OF CHROMOSOMAL DAMAGE INDUCED IN RESTING RAT-LIVER CELLS BY X-RAYS AND 4.2-MEV NEUTRONS.

**Tates AD, Broerse JJ, Neuteboom I, De Vogel N**
**Dept. Radiation Genetics and Chemical Mutagenesis, Sylvius Lab., Wassenaarseweg 72, 2333 AL Leiden, The Netherlands**
**Mutat Res; 92(1/2):275-290 1982**

Young male Wistar rats (35-45 days old) or mature WAG/Rij female rats (24 wk old) were exposed to total-body irradiation with x-rays (XR: 100-400 rads) or 4.2 million electron volt neutrons (NR: 25-100 rads). Partial hepatectomy was performed 1 day-3 mo after irradiation; 2-3 days postoperatively, the remaining liver was perfused and isolated hepatocytes were examined for cytoplasmic micronuclei. Both XR and NR caused a dose-related increase in the occurrence of micronuclei. The plateau of the dose-effect curve was observed at 400 rads XR and 50 rads NR. In the XR group, the frequency of micronucleated hepatocytes decreased with increasing time intervals after irradiation; the frequency at 3 mo was not significantly different from the control value. In the NR group, the frequencies of micronucleated hepatocytes remained constant at all time intervals studied. The progressive decline in the frequencies of hepatocytic micronuclei after XR exposure may be explained by two mechanisms operating simultaneously: slow, long-term repair of chromosomal damage and mitotic selection against cells bearing substantial amounts of chromosomal damage. The mechanisms did not seem to be in effect in the NR group. The relative biologic effectiveness of NR in the ascending portion of its dose-effect curve was about 4 relative to XR. The long-term effects of XR and NR should be compared at lower doses, at which cell regeneration induced by XR is not demonstrable. Such experiments might provide more information on possible long-term repair processes in resting (GO) liver cells with XR-induced chromosomal damage. (26 Refs)

### 16. CELL INJURY AND DNA REPAIR IN X- AND NEUTRON-IRRADIATED CHINESE HAMSTER CELLS.

**Korner IJ, Tolkendorf E, Handschack W, Malz W**
**Central Inst. Molecular Biology, Acad. Sciences GDR, Lindenberger Weg 70, DDR-1115 Berlin, E. Germany**
**Stud Biophys; 86(1):81-82 1981**

Survival rates and chromosome aberrations under oxic and hypoxic conditions and DNA single- and double-strand break rejoining in x- and neutron-irradiated Chinese hamster cells under oxic conditions were investigated. Relative biological effectiveness (RBE) decreased with increasing neutron dose. Survival curves provided an oxygen enhancement ratio of approx 3.0 after x- and 1.9 after neutron-irradiation. The results of chromosome aberration induction provided the highest RBE for asymmetrical chromosomal exchanges dependent on neutron dose. The higher RBE of the fast neutrons concerning the survival correlated with the rate of chromosome breaks and DNA double-strand breaks and also with a decreased rejoining of single- and double-strand breaks. (5 Refs)

### 17. EFFECTS OF BETA RADIATION ON AMPHIBIAN EMBRYOS (PLEURODELES WALTLII) AND CAPACITIES OF REGULATION DURING DEVELOPMENT.

**Gallien CL, Lenfant-Guyot M, Labrousse JP**
**Laboratoire de Biologie du Developpement, Universite Rene Descartes, 45, rue des Saints Peres, 75270 Paris Cedex 06, France**
**Radiat Phys Chem; 18(3/4):609-617 1981**

Effects of beta-radiation on larvae of the salamander, Pleurodeles waltii, were examined at the cellular level after exposure to 70 rad. Doses between 70 rad and the 100% lethal dose of 500 rad only caused structural changes in chromosomes, with no relationship between dose and type of abnormality produced. However, the number of cells presenting with abnormalities of karyotype increased in relation to dose. During development after radiation, cells with major abnormalities may be eliminated and healthy cells, or those with abnormalities compatible with normal mitotic activity, seem to be preserved. (6 Refs)

### 18. SOME NOTIONS ABOUT CONNECTION OF RADIOSENSITIVITY WITH STATIONARY STATES OF CHROMATIN.

**Spitkovsky DM, Andreev SG**
**Inst. Medical Genetics, Kashirskoe shosse 6a, USSR-115 478 Moscow, USSR**
**Stud Biophys; 86(1):83-84 1981**

The physical mechanism of intensification of the radiation damaging action on chromatin was discussed and an attempt to explain the mechanism according to hypothesis for chromatin stationary states was made. Radiation of fixed human lymphocytes by alpha-particles (Pu239) at small doses confirms the suggested hypothesis predicting chromatin transition between states under radiation with 0.07-0.1 Gray Units (Gy) or 0.7-1 Gy. Microdosimetric analysis showed that only single DNA molecules were damaged at the doses used and no radiation depolymerization of chromatin in nuclear vol occurred. One of the possible explanations of transition mechanism is a chromatin model consisting of 'beads interacting on a torsion fiber'. (4 Refs)

## OTHER CELLULAR EFFECTS OF IRRADIATION

### 19. FAILURE OF RNA SYNTHESIS TO RECOVER AFTER ULTRAVIOLET IRRADIATION: AN EARLY DEFECT IN CELLS FROM INDIVIDUALS WITH COCKAYNE'S SYNDROME AND XERODERMA PIGMENTOSUM.

**Mayne LV, Lehmann AR**
**(c/o Lehmann) MRC Cell Mutation Unit, Univ. Sussex, Falmer, Brighton, Sussex BN1 9QG, England**
**Cancer Res; 42(4):1473-1478 1982**

Previous work has shown that in cells from the UV-sensitive genetic disorder, Cockayne's syndrome, DNA synthesis fails to recover after UV irradiation, despite the fact that these cells have no detectable defect in either excision or daughter-strand repair pathways. We now show that Cockayne cells, as well as cells from a number of patients with xeroderma pigmentosum, are sensitive to the lethal effects of UV irradiation in stationary phase under conditions in which no DNA is synthesized after irradiation. Furthermore, in normal and defective human fibroblasts, RNA synthesis is depressed after UV irradiation. In normal (dividing) cells, RNA synthesis recovers very rapidly, but this recovery does not occur in Cockayne cells, and it is reduced or absent in xeroderma pigmentosum cells from different complementation groups. Qualitatively, similar results are obtained with cells in stationary phase. The recovery of RNA synthesis in the various defective cell strains is not correlated with the overall extent of excision repair, but there is some correlation between recovery of RNA synthesis and cell survival after UV irradiation. These results implicate recovery of RNA synthesis as an important early response to UV irradiation. (Author abstract) (33 Refs)

## THEORETICAL ASPECTS OF RADIATION CARCINOGENESIS

### 20. EVOLVING PERSPECTIVES ON THE EPIDEMIOLOGY AND BIOLOGY OF CANCER: NEEDS AND OPPORTUNITIES.

**Upton AC**

**Inst. Environmental Medicine, New York Univ. Medical Center, New York, NY**

**Cancer Research in the People's Republic of China and the United States of America: Epidemiology, Causation and New Approaches to Therapy, Proceedings of a Conference held in New York, 28-29, March, 1980. Marks PA, ed. New York, Grune and Stratton, 273 pp., 1981.**

Differences in the incidence of cancer (CA) in different parts of the world are presented and the needs and opportunities of research in the epidemiology and biology of CA are discussed. Assumed parameters of a model for estimating CA risks associated with low-level ionizing radiation, estimated risks of radiation-induced CA, and estimates of the annual contribution of radiation exposure to the lifetime burden of fatal CA to the United States (US) population are presented. Time-trends in lung CA mortality and cigarette consumption in England and Wales; incidence of lung CA in regular cigarette smokers in relation to the number of cigarettes smoked/day; time-trends in CA death rates in US males standardized for age; and dose-incidence curves for breast CA in relation to radiation exposure in women surviving atomic-bomb radiation, women treated with x-rays for acute postpartum mastitis, and women subjected to multiple fluoroscopic examinations for pulmonary tuberculosis are presented. (15 Refs)

### 21. METHOD OF ANALYSIS OF MONOTONE DOSE-RESPONSE PROBABILITIES AFTER LONG-TERM EXPOSURE TO A TOXICANT.

**Scott BR**

**Inhalation Toxicology Res. Inst., Lovelace Biomedical and Environmental Res. Inst., P.O. Box 5890, Albuquerque, NM, 87185**

**Health Phys; 42(3):305-315 1982**

A nonparametric hazard-function (HP) method for generating monotonically increasing incidence vs dose curves after long-term exposure to a toxic agent (eg radiation or chemical carcinogens) is described in detail in this paper. Here, incidence refers to the response-probability estimate that is adjusted for competing risks. The maximum likelihood principle was used to arrive at an appropriate point estimate of the cumulative hazard function (ie the negative natural logarithm of the proportion of nonresponders) and the response probability for an array of doses that depends on the data set to be analyzed. The resultant point estimates can be used to develop or select an appropriate model for risk vs dose assessment. As an example of the application of the HF method, data for liver neoplasms caused by long-term exposure of mice to 2-acetylaminofluorene and data for radiation pneumonitis and pulmonary fibrosis caused by long-term exposure of dogs to ionizing radiation are analyzed. (Author abstract) (15 Refs)

### 22. DOSE-MORTALITY RELATIONSHIPS IN RFM MICE FOLLOWING 137CS GAMMA-RAY IRRADIATION.

**Prentice RL, Peterson AV, Marek P**
**Dept. Biostatistics, Univ. Washington, Seattle, WA, 98105**
**Radiat Res; 90(1):57-76 1982**

The usefulness of mortality rate function estimation for exploration and display of dose-mortality data with competing risks is demonstrated with data from single-exposure 137Cs gamma-irradiated RFM/Un mice (16,199 females; 2,032 males). Use of a proportional-hazards regression technique allowed quantification of mortality rates as a function of both radiation dose and animal age. Data is reported for five tumor types: thymic lymphoma, myeloid leukemia, reticulum cell sarcoma, ovarian tumor, and lung tumor. The relative risks as estimated by the linear, quadratic, linear time-dependent, and quadratic time-dependent models using all doses are compared. For most mortality types, relative risks were linear as a function of dose and decreased markedly with increasing time after exposure; the exception being ovarian cancer for which mortality rate increased sharply and nonlinearly for doses as low as 50 rad and elevated relative risks did not decline as the animals aged. The age-specific relative risks were similar in all mice, despite different overall relative risks for male and female mice at particular doses. Thus, a unified dose-response model for all natural causes of mortality was obtained. Implications of the analyses for low-dose extrapolation are discussed. (14 Refs)

### 23. SOME CONCEPTS, TERMINOLOGY, AND METHODOLOGY FOR RADIATION RISK ASSESSMENT.

**Groer PG, Barlow RE**
**Inst. for Energy Analysis, Oak Ridge Associated Universities, Oak Ridge, TN, 37830**
**Radiat Res; 90(1):35-40 1982**

Definitions of some probabilistic concepts that will help to rigorously define dose-response curves are presented. The frequentist and the Bayesian approaches to statistics are used to estimate certain probabilities and/or related quantities from information concerning observed mortality times and types of subjects exposed to a particular amount of radiation. Advantages and disadvantages of the approaches are discussed. The Bayesian approach assesses uncertainty about unknown parameters probabilistically with the help of density functions, rather than providing potentially meaningless point estimators. (16 Refs)

### 24. FAILURES AND CRITIQUE OF THE BEIR III LUNG CANCER RISK ESTIMATES.

**Cohen BL**
**Univ. Pittsburgh, Pittsburgh, PA, 15260**
**Health Phys; 42(3):267-284 1982**

The BEIR III prediction of lung cancer incidence due to environmental radon is more than twice the actual incidence of all lung cancers among non-smokers. No more than 10% of all lung cancers in non-smokers can be due to radon. When alternative causes of lung cancer are considered the BEIR III estimates of lung cancer risk due to environmental radon are too high for non-smokers by at least a factor of 40. The evidence for synergism between smoking and radiation induced lung cancer is reviewed, and the BEIR III estimates for smokers are too high by at least a factor of 10. The bases for the BEIR III model are reviewed, and it must be based almost entirely on the Czechoslovakian uranium miners; its estimated risks are higher than would be obtained from all other studies. The possibility that there are other causes than radon for lung cancer among miners is discussed. Other causes can easily explain all cases where lung cancer rates are high, but it is very difficult to explain the much lower rates for US uranium miners (5x lower than BEIR III estimates) and other similar situations. The BEIR III lung cancer model is strongly supra-linear (ie concave downward), contrary to the bulk of experimental and theoretical evidence on that question, and contrary to other statements in the BEIR III Report. The BEIR III lung cancer risk estimates are probably too high by a factor of 2-5 for miners, and because of different smoking habits, the risk to the public may be another factor of 2 lower. The remainder of the overestimate for effects of environmental radon must be due to non-linearity in the dose-response relationship. (56 Refs)

### 25. THE BEIR III REPORT: A REVIEW.

**Paris OH**
**Nuclear Regulatory Commission, Washington, DC, 20555**
**Nucl Saf; 22(5):626-635 1981**

The final edition of the BEIR III report was published in late November 1980. An original draft version had been released in May 1979, but that version contained a 'Dissenting Report,' which said that the risk of radiation-induced cancer had been exaggerated. After many members of the BEIR III Committee indicated their agreement with the dissent, the chapter on cancer was substantially revised. Nevertheless, that chapter still contains dissenting opinions in the final edition. Cancer risk from low-level, low linear energy transfer (LET) radiation was estimated in BEIR III using a linear-quadratic function to extrapolate to low doses from more reliable data at high dose levels. Upper- and lower-bound estimates were derived using the linear model and the pure quadratic model, respectively. The linear-quadratic estimates, considered by the Committee to be scientifically more plausible, were consistently less than comparable risk estimates obtained from the 1972 BEIR I report, which used the linear hypothesis. Genetic risk was estimated in BEIR III using some methods and assumptions similar to those used in BEIR I, including use of the linear hypothesis. New information available since 1972 contributed to refinements in making risk estimates. The BEIR III Committee noted, however, that radiation-induced transmitted genetic effects still have not been demonstrated in man; so genetic risk estimates must be based on experiments with laboratory animals. The BEIR III estimates of genetics risk are not notably different from those in BEIR I. (Author abstract) (8 Refs)

## ENVIRONMENTAL RADIATION AND PROTECTION STANDARDS

### 26. ASSESSMENT OF THE IN VITRO RADIOSENSITIVITY OF HUMAN PERIPHERAL BLOOD LYMPHOCYTES.

**Knox SJ, Shifrine M, Rosenblatt LS**
**Lab. Energy-Related Health Res., Univ. California, Davis, Davis, CA, 95616**
**Radiat Res; 89(3):575-589 1982**

Sensitivities of different assay methods used to study the effects of low-level (sublethal) in vitro x-irradiation on lymphocytes were evaluated. Sensitive lymphocyte progenitor cells from 31 clinically normal adults were evaluated for proliferative capacity following in vitro x-irradiation at 0-400 R. Dose-response studies were conducted using human whole blood and gradient-separated lymphocyte enriched mononuclear cell fractions in the lymphocyte stimulation test (LST) and colony formation assay (Col) with six different mitogens/antigens. Assays using whole blood were able to detect radiation effects at lower doses than assays using gradient-separated cells. Col was consistently more sensitive than LST with mitogen/antigen groups. Survival curves for subjects based on LST results were characterized by a typical dose-response curve with a shoulder at lower doses followed by a single-exponential decrease in survival; the number of colonies relative to dose followed a two-exponential curve lacking a shoulder at lower doses. The assays are potentially applicable to assessment of the relative radiosensitivity of lymphocytes and associated risk for radiation-induced leukemogenesis of different population groups with immunologic and hematologic abnormalities. (46 Refs)

### 27. NEPTUNIUM - THE NEGLECTED ACTINIDE: A REVIEW OF THE BIOLOGICAL AND ENVIRONMENTAL LITERATURE.

**Thompson RC**
**Biology Dept., Pacific Northwest Lab., Richland, WA 99352**
**Radiat Res; 90(1):1-32 1982**

Biological and environmental behavior and biomedical effects of isotopes of neptunium are reviewed. Potential sources of human exposure are fallout from nuclear weapons, effluent cooling water from fission reactors, industrial processing of 237Np produced in fission reactors, and its presence as a long-lived component of high-level nuclear wastes. Due to a long half-life, and because Np is more environmentally and physiologically available than other heavy-metal alpha emitters, 237Np has been estimated to be the most hazardous material remaining in waste from about 10,000 yr to 30 million yr after disposal. Measurements of Np in the environment are described. Experimental studies relating to Np in the environment are reviewed with respect to environmental chemistry and the food chain. Animal biokinetic studies involving absorption from and retention in the gastrointestinal tract, lung, skin, sc tissues, and deposition and retention in systemic organs (blood, bone, liver, kidney, spleen, adrenal, gonads, placenta-fetus, other tissues, excreta, and enhanced excretion) are discussed. Early and late effects of Np exposure in animal toxicity studies are presented. Evidence indicates that Np might be more carcinogenic than other actinides, possibly due to chemical effects supplementing radiation effects. The potential hazard of Np exposure to humans is discussed, and exposure limits as outlined by the International Commission on Radiological Protection are reported. (89 Refs)

### 28. ON THE RADIOLOGICAL SIGNIFICANCE OF INHALED URANIUM AND THORIUM ORE DUST.

**Hannibal L**
**Natl. Inst. Radiation Hygiene, Frederikssundsvej 378, DK-2700 Bronshoj, Copenhagen, Denmark**
**Health Phys; 42(3):367-371 1982**

The risk ensuing from inhalation of uranium and/or thorium bearing particles was evaluated by calculating the resulting effective committed dose equivalent. In mines, if respiration protection is not worn, radioactive ore dust may represent an important health physics problem. Oral intake of finely divided ore material does not appear to present a comparable problem. Accurate determination of the cumulative dust exposure is important for workplaces in the uranium and thorium mining industry. Personal respirable air monitors should be used for the most heavily exposed workers. Determination of the actual particle size is necessary to provide a more realistic risk evaluation. (4 Refs)

### 29. INHALATION EXPOSURES AT A THORIUM REFINERY.

**Mausner LF**
**Medical Dept., Brookhaven Natl. Lab., Upton, NY, 11973**
**Health Phys; 42(2):231-236 1982**

Exposure of workers at a thorium refinery to 232-thorium was studied. Analysis of air filter samples indicated geometric mean airborne concentrations of .0071-.072 picoCi/liter (pCi/l), compared with a max permissible level of .030 pCi/l. Examination of autopsy specimens from two workers indicated significantly increased levels of 232-thorium compared with individuals not occupationally exposed to 232-thorium. Also sometimes present in increased levels in the air and in tissue samples were 220-radon, 212-lead, 212-bismuth, and rare earth elements. (15 Refs)

### 30. A REVIEW OF TRANSFER FACTORS FOR ASSESSING THE DOSE FROM RADIONUCLIDES IN AGRICULTURAL PRODUCTS.

**Ng YC**
**Environmental Sciences Div., Lawrence Livermore Natl. Lab., P. O. Box 5507, Livermore, CA, 94550**
**Nucl Saf; 23(1):57-71 1982**

The dose to man from radionuclides released to the environment is generally assessed with mathematical models that require transfer factors as input parameters to predict the concentration of radionuclides in foodstuffs. This article summarizes recent attempts to review the worldwide literature and derive updated transfer factors to predict concentrations of radionuclides in terrestrial foods using equilibrium models. Updated transfer coefficients to predict the concentration of a radionuclide in cow's milk and other animal products from that in feed are presented as well as concentration factors to predict the concentration of a nuclide in a food or feed crop from that in soil. Comparing the updated transfer coefficients with those in existing tables leads to suggested changes in the transfer coefficients for milk and beef. Soil-to-plant concentration factors are extremely variable, which limits the usefulness of a single concentration factor to predict the uptake of a radionuclide into crops from soil. The potentially large uncertainty associated with predicting the uptake of radionuclides by plants from soil at a particular location may be reduced by considering the dominant crops and soil types in the area and how various soil properties affect the concentration factor. The updated transfer factors may be useful in assessing transport through terrestrial food chains when site-specific information is not available. In addition, they provide a basis for systematically updating existing tables of transfer factors for generic assessments. (Author abstract) (48 Refs)

### 31. SOME COMMENTS ON BEIR III.

**Stoll E, Chakraborty S**
**Nuclear Safety Div., Radiation Protection Section, CH-5303, Wurenlingen, Switzerland**
**Health Phys; 42(2):225-226 1982**

We compared the dose-equivalent concept of the ICRP with the data published in BEIR III. It is obvious that some of the numbers arrived at in BEIR III differ from those published by the ICRP, particularly with regard to the proportion of the total risk due to irradiation of the breast and lung. The possible significance of these differences is shortly discussed. (Author abstract) (5 Refs)

### 32. THE CURIOUS CASE OF THE RADIOACTIVE RING.

**Stearns FW**
**Tulsa, OK**
**J Am Acad Dermatol; 5(6):696-697 1981**

Radioactivity discovered in gold jewelry, particularly rings, has caused cancer and has necessitated excision, grafting, chemotherapy, and amputations. The first contaminated ring was identified in 1940; since then, many pieces of jewelry have been identified, mostly in New York or northwestern Pennsylvania. However, new pieces have been found in other parts of the country and Canada. The conclusion, in 1969 by the Bureau of Radiological Health, that radioactive contamination of gold from spent radon seeds is not a widespred public hazard, is not acceptable. (6 Refs)

## REVIEWS AND OTHER STUDIES

### 33. ANTITUMOR EFFECT OF RETINOIDS.

**Mahrle G, Berger H**
**Universitats-Hautklinik, v. Siebold-Str. 3, D-3400 Gottingen, W. Germany**
**Z Hautkr; 57(6):429,430,433 1982**

The potential value of retinoids in the treatment of skin tumors is discussed. Experiments in animals have shown that high doses of retinoids have antitumor effects against malignancies induced by viruses, chemicals, ionizing radiation, and UV radiation. It is noted that these experiments also revealed that extremely high doses of retinoids can cause promotion of tumor growth. This cocarcinogenic effect was most pronounced with UV-radiation induced tumors; doses as low as 0.01% and 0.001% have been reported to enhance tumor growth. In rabbits treated topically with dimethylbenzanthracene (DMBA), 20-30 mg of aromatic retinoids per day per animal was found to inhibit tumor growth. Despite the experimental findings, retinoids are not widely used in the treatment of human cancer. It is suggested that they could be valuable in the treatment of basal cell carcinoma, squamous cell carcinoma, and melanoma. It is concluded that retinoids will be used in the future as adjuvant therapy for reducing the size of tumors or preventing recurrences. (15 Refs) (In GER)

### 34. THE ETIOLOGY, EPIDEMIOLOGY, AND PREVENTION OF LUNG CANCER.

**Wynder EL**
**American Health Foundation, 320 East 43rd St., New York, NY, 10017**
**Semin Respir Med; 3(3):135-139 1982**

The risk of lung cancer increases proportionally with the number of cigarettes smoked/day and the number of yr smoked. Smoking is the primary cause of lung cancer. Epidemiologic studies have suggested that risk of lung cancer decreases with reductions in the amount of tar in cigarettes smoked. Occupational exposure to asbestos, uranium, arsenic, coal products, bischloromethyl ether, vinyl chloride, nickel, chromium, iron oxide, and mustard gas is also associated with an increased risk of lung cancer. Some occupational exposures work synergistically with tobacco smoke. The higher rate of lung cancer in cities than rural areas can be explained by higher frequency of smoking, more occupational exposure to carcinogens, and higher reporting of lung cancer. The relationship between passive inhalation of cigarette smoke and lung cancer is unproven. Lung cancer can be prevented by preventing smoking in children, the cessation of smoking by adults, and by developing less harmful cigarettes. (15 Refs)

### 35. LUNG CANCER AND OCCUPATIONAL LUNG DISEASE.

**Weiss W**
**Room 6401 New Coll. Building, Hahnemann Medical Coll., 230 North Broad St., Philadelphia, PA, 19102**
**Clin Chest Med; 2(2):289-300 1981**

Epidemiology and etiology, natural history, diagnosis, therapy, and prognosis of lung cancer and occupational lung disease are discussed. Lung cancer has been associated with cigarette smoking and occupational causes such as asbestos exposure, ionizing radiation, and chemicals. Early detection and treatment have produced disappointing results, indicating that in most cases invasion and metastasis have occurred well before the 30th doubling. (65 Refs)

### 36. SOLAR RADIATION AND MALIGNANT MELANOMA OF THE SKIN.

**Houghton AN, Viola MV**
**Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021**
**J Am Acad Dermatol; 5(4):477-483 1981**

Solar radiation is discussed in relation to the pathogenesis of malignant melanomas (MM) of the skin. The incidence of MM in relatively homogeneous white populations in North America, northern Europe, and Australia is inversely proportional to latitude. MM tends to occur on sites more heavily exposed to sun during recreation. MM is more likely to develop in lightly pigmented individuals. Susceptible persons who have lived in a sunny climate all of their lives have a higher incidence of MM than persons who have recently moved to the same area from less sunny climates. A higher incidence of MM seems to occur in areas with extensive coastlines. MM is more frequent in the summer. MM rates are considered in terms of indoor and outdoor occupations. Sunspot cycles seem to be correlated with subsequent increases in MM incidence rates. Max sunspot numbers coincide with periods of increased solar activity. The rise in MM incidence 0-3 yr after sunspot peaks suggests that heavier exposures to UV radiation trigger the clinical appearance of MM. Solar radiation is considered as a dose-dependent carcinogen and as a cocarcinogen or promoter. (34 Refs)

### 37. MELANOMA OF THE SKIN: SOME EPIDEMIOLOGICAL ASPECTS.

**Green A**
**Queensland Inst. Medical Res., Australia**
**Aust Fam Physician; 11(1):7-12 1982**

Epidemiological aspects of melanoma of the skin are reported. The incidence and mortality rate of cutaneous melanoma is increasing in several countries. Types of melanoma include Hutchinson's melanotic freckle, superficial spreading melanoma, nodular melanoma, and acral lentiginous melanoma. Sun exposure is causally related to melanoma and depends on latitude, skin pigment, and body site exposed. Other etiological factors include hormones, socioeconomic status, and heredity. Current preventive concepts include awareness of characteristics of UV radiation, protective clothing, and use of sunscreens. (29 Refs)

### 38. CANCER. AN INTRODUCTION.

**Creasy WA**
**Dept. Pharmacology, Univ. Pennsylvania Sch. Medicine, Philadelphia, PA**
**Cancer. An Introduction. New York, Oxford University Press, 271 pp., 1981.**

Nature and incidence of cancer (CA), the features of CA growth and metastasis, the biological interactions between the tumor and the host, the principles of diagnostic approaches, the various factors known or suspected to produce CA, the forms of treatment, and some of the major direction s of CA research are presented. Classification of tumors and growth disorders, grades and stages, differentiation, dedifferentiation, and mutation are discussed. Comparative neoplasia, historical aspects of human CA, modern incidence and trends in incidence of CA, and probability of developing CA are reviewed. Host-tumor relationships as manifested in cachexia, pain, hormonal and other humoral factors, psychological aspects, and miscellaneous complaints are considered. Detection and diagnosis of CA consist of self-examination, surgical and cytological diagnosis, radiological tests, direct inspection of lesions, biochemical diagnostic tests, and immunological diagnosis. The etiology of CA includes genetic factors in CA development, psychological, immunological, endocrinological, and metabolic aspects of CA development, chemical, radiation, and miscellaneous mechanisms of carcinogenesis, and viral etiology of CA. Surgery, radiotherapy, chemotherapy, and immunotherapy are used in CA treatment. Unproven and dietary treatments for CA are those with laetrile, dietary regimens, vitamin therapy, and some other unproven and folk remedies. The CA research endeavor in drug development, clinical trials, and some recent areas of research activity in therapeutics are reviewed. (710 Refs)

### 39. CAUSES OF LEUKEMIAS AND CANCER: RECENT PROGRESS.

**Bernard J**
**bd. de Perolles 53, 1700 Fribourg, Switzerland**
**Rev Med Suisse Romande; 102(1):95-103 1982**

Roles of viruses, radiation, and toxic chemical substances in the development of cancer are discussed. Burkitt's lymphoma (BL), a B-cell lymphoma predominantly localized in facial bones and found most frequently in certain areas of Africa, was one of the first cancers to be related to a virus, Epstein Barr virus (EBV). EBV virus and its antibodies are found in BL patients. EBV virus, the infective agent in mononucleosis, has been shown to cause BL in marmosets. BL shows high correlations with geographic areas with levels of malaria, with chromosome translocation 8:14, and with lower socioeconomic groups. Viruses have also been implicated in cervix cancer (herpes virus), liver cancer (hepatitis B), and Hodgkin's disease. Evidence of radiation-induced cancers has been gained from studies of physicians, radiologists, and scientists exposed to radiation and of Hiroshima survivors. The relationship between radiation and cancer development is significant but varies among individuals. Dietary factors, such as tobacco (lung, bladder, and digestive cancers), alcohol (cirrhosis and liver cancer), and diet in general (high lipid diet and breast cancer) have been related to increased incidences of cancer. Leukemia has been observed in Hodgkin's disease patients treated with chemotherapy. A high incidence of lymphomas has been noted in patients who have undergone organ transplants. The role of heredity and geography in the etiology of cancer is dis cussed. (no Refs) (In FRE)

### 40. RADIOLOGICAL PROTECTION IN HEALTH CARE.

**Ramsdale ML, Horton PW**
**Dept. Medical Physics and Bio-Engineering, RKH Programme, Riyadh, Saudi Arabia**
**Saudi Med J; 3(1):9-16 1982**

Radiation and effects, principles of radiation protection in radiology, radiotherapy, nuclear medicine, and monitoring on the effectiveness of the protection arrangements are described. The most important late effect of radiation is cancer. Risk estimates are complicated by the long latent period and by the relatively small numbers involved. Irradiation at an early stage of pregnancy can lead to abnormal development, and irradiation of the fetus can result in an increased risk of childhood cancer. The aim in radiotherapy is to deliver an accurate given dose to malignant tissue without causing damage to surrounding tissues. Because of the high-dose rates involved, stringent measures are required to ensure the safety of staff and the proper treatment of patients. (1 Ref)

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| PHILIP C. HANAWALT<br>Stanford University | *Cellular Responses to Damaged DNA* | #VK03<br>54 min. |
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1. IARC MONOGRAPHS ON THE EVALUATION OF THE CARCINOGENIC RISK OF CHEMICALS TO MAN. SOME ANTINEOPLASTIC AND IMMUNOSUPPRESSIVE AGENTS.
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IARC Mongr Eval Carcinog Risk Chem Hum 26: 411 pp., 1981.

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Dept. Pharmacology, Thomas Jefferson Univ., Philadelphia, PA, 19107
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Drug Chem Toxicol; 4(3):185-195 1981

4. HORMONES AND BREAST CANCER.
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Dept. Biology, McGill Univ., 1205 Ave. Docteur Penfield, Montreal H3A 1B1, Canada
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## OTHER REVIEWS IN CARCINOGENESIS

39. MATHEMATICAL MODELS OF THE CELL CYCLE WITH A VIEW TO TUMOR STUDIES.
Bertuzzi A, Gandolfi A, Giovenco MA
Centro di Studio dei Sistemi di Controllo e Calcolo Automatici del C.N.R., Via Eudossiana 18, 00184 Rome, Italy
Math Biosci; 53(3/4):159-188 1981

**40. NEOPLASMS IN DOMESTIC ANIMALS: A REVIEW OF EXPERIMENTAL AND SPONTANEOUS CARCINOGENESIS.**
**Madewell BR**

Section Clinical Oncology, Dept. Veterinary Surgery, Univ. California, Davis, CA, 95616

Yale J Biol Med; 54(2):111-125 1981

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# RADIATION CARCINOGENESIS

SERIES CK06 No. 82/09

SEPTEMBER, 1982

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**U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES**
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## RADIATION CARCINOGENESIS IN HUMANS

### 1. MORTALITY STATISTICS AMONG ATOMIC BOMB SURVIVORS IN HIROSHIMA PREFECTURE, 1968-1972.

**Kurihara M, Munaka M, Hayakawa N, Yamamoto H, Ueoka H, Ohtaki M**
**Dept. Epidemiology and Social Medicine, Res. Inst. for Nuclear Medicine, and Biology Hiroshima Univ., 2-3 Kasumi 1-chome, Minami-ku, Hiroshima 734, Japan**
**J Radiat Res (Tokyo); 22(4):456-471 1981**

Mortality among the approx 160,000 atom bomb survivors in Hiroshima during the period 1968-72 due to selected causes of death, including malignant neoplasms, is discussed. In terms of all causes of death, the relative risk of survivors was 0.913, which is significantly lower than for the non-exposed population. The risk of survivors for malignant neoplasms, however, was 16% higher than for non-exposed individuals. The risk of some neoplasms was significantly elevated in the survivor population: leukemia, lymphosarcoma, reticular cell sarcoma, and cancer of the large intestine, testis, ovary, and larynx. Other neoplasms, such Hodgkin's disease, carried a lower risk. Among non-neoplastic causes of death, diseases of the blood and blood-forming organs, hypertensive diseases, and others are at a significantly higher risk in the exposed group whereas senility, gastroenteritis, and accidents are all significantly lower. (11 Refs)

### 2. LUNG CANCER AMONG NAVAJO URANIUM MINERS.

**Gottlieb LS, Husen LA**
**2-116 East Cliff Drive, Santa Cruz, CA, 95062**
**Chest; 81(4):449-452 1982**

The contribution of smoking habits and uranium mining experience to the lung cancer origin in 16 adult male Navajo patients was assessed. The mean age of death of the 15 deceased miners was 46.1 yr (range 31-70 yr); the 16th miner was alive at 52 yr. The mean length of time of exposure in the mines was 11.9 yr (range 0.5-23 yr). The mean induction-latent period was 15 yr (range 5-30 yr). Ten of the miners had small cell undifferentiated cancer and three had epidermoid type. Fourteen miners were nonsmokers and two were light to moderate smokers. Survival time of the deceased nonsmokers was 1 day to 24 mo, and for the smokers 5-9 mo. There was no correlation between induction-latent period and either time in mines or cumulative exposure to irradiation (CER). The mean CER was 1,139.5 working level mo (range 58.8-2,125). Cigarette smoking is assessed a promoting role in acquisition of lung cancer by uranium miners as two of the three miners with latency periods less than 11 yr were smokers. Radiation was the major cancer initiating agent in these patients. (19 Refs)

### 3. EFFECTS OF LOW-DOSE RADIATION. A CORRELATION STUDY.

**Edling C, Comba P, Axelson O, Flodin U**
**(c/o Axelson) Dept. Occupational Medicine, Univ. Hosp., S-581 85 Linkoping, Sweden**
**Scand J Work Environ Health; 8(Suppl1):59-64 1982**

Based on information in the literature, five types of malignancies (lung, breast, and pancreatic cancer, leukemia, and multiple myeloma) probably respondent to irradiation induction and therefore likely to correlate with background radiation were chosen for the correlation study on effects of low-dose radiation. Mortality rates age-standardized directly for lung and breast cancer and leukemia during 1969-1978 and for pancreatic cancer and multiple myeloma during 1961-1973 in the counties of Sweden and for persons 40 yr old and over, along with estimates of background radiation (cosmic radiation excluded), Pearson coefficients and p-values are presented. Significant correlation was observed between the estimates of background radiation and lung cancer, for both males and females. A similar correlation was observed for pancreatic cancer in both sexes. Leukemia showed a correlation of borderline significance for males and a weaker correlation for females. Breast cancer (in women only) and multiple myeloma did not show any significant correlation. Risk estimates for lung cancer per working level mo (WLM) and per 10(6) person-yr for persons greater than 50 yr old in various Swedish populations (including Zn-Pb miners) and estimates given in a previous report indicate that 25-35 cases per 10(6) person-yr and per WLM might result from radon daughter exposure. (31 Refs)

### 4. DIRECT ESTIMATES OF LOW-LEVEL RADIATION RISKS OF LUNG CANCER AT TWO NRC-COMPLIANT NUCLEAR INSTALLATIONS: WHY ARE THE NEW RISK ESTIMATES 20 TO 200 TIMES THE OLD OFFICIAL ESTIMATES?

**Bross ID, Driscoll DL**
**Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263**
**Yale J Biol Med; 54(5):317-328 1981**

An official report on the health hazards to nuclear submarine workers at the Portsmouth Naval Shipyard (PNS), who were exposed to low-level ionizing radiation, was based on a casual inspection of the data and not on statistical analyses of the dosage-response relationships. When these analyses are done, serious hazards from lung cancer and other causes of death are shown. As a result of the recent studies on nuclear workers, the new risk estimates have been found to be much higher than the official estimates currently used in setting NRC permissible levels. The official BEIR estimates are about one lung cancer death per yr per million persons per rem. The PNS data show 189 lung cancer deaths per yr per million persons per rem. (Author abstract) (15 Refs)

## EXPERIMENTAL RADIATION CARCINOGENESIS

### 5. FREQUENCY OF UV-INDUCED NEOPLASTIC TRANSFORMATION OF DIPLOID HUMAN FIBROBLASTS IS HIGHER IN XERODERMA PIGMENTOSUM CELLS THAN IN NORMAL CELLS.

**Maher VM, Rowan LA, Silinskas KC, Kateley SA, McCormick JJ**
**Carcinogenesis Lab., Michigan State Univ., Fee Hall, East Lansing, MI, 48824**
**Proc Natl Acad Sci USA; 79(8,part1):2613-2617 1982**

If neoplastic transformation of diploid human cells results from carcinogen-induced mutations, cells deficient in excision repair of UV-induced DNA damage should be significantly more sensitive to transformation by UV light than normal cells. We tested this hypothesis by irradiating fibroblasts from a xeroderma pigmentosum patient (XP7BE, complementation group D) with low doses of UV light (254 nm) and cells from a normal person with much higher doses and comparing the frequency of transformation to anchorage independence. Both sets of cells exhibited a dose-dependent increase in transformation which corresponded to a dose-dependent decrease in survival.

At doses that caused equal cell killing, the frequency of anchorage-independent cells was approximately equal. Colonies of XP7BE and normal cells isolated from agar, propagated, and injected into x-irradiated athymic mice produced fibrosarcomas in 100% of the animals. Normal cells irradiated shortly before the onset of DNA synthesis exhibited a high frequency of anchorage-independent cells; cells irradiated in early G1 showed no increase over background. These results agree with those we observed for UV induction of 6-thio-guanine-resistant mutants in these cells and support the hypothesis that anchorage independence results from mutations induced by DNA replication on a damaged template. (Author abstract) (21 Refs)

### 6. PARENTAL EXPOSURE TO X RAYS AND CHEMICALS INDUCES HERITABLE TUMOURS AND ANOMALIES IN MICE.

**Nomura T**
**Inst. for Cancer Res., First Dept. Surgery, Osaka Univ. Medical Sch., Fukushima-ku, Osaka 553, Japan**
**Nature; 296(5857):575-577 1982**

A summary is presented of the effects of radiation (RT) with x-rays and various chemical in mice studied in multiple generations over a 13-yr period and involving 12,905 live-born mice and 9,645 fetuses from 2,904 parents. There was almost a linear increase in dominant lethals following radiation (RT) of spermatids, spermatozoa, and oocytes. There was no significant increase after treatment of spermatogonia. No increase in dominant lethals was produced by treatment with urethan (U). There was a large and significant increase in anomalies in progeny of parents treated with RT or U; only open eyelid, the predominant non-lethal anomaly, was shown to be transmissible. Both RT and U significantly increased the number of tumors in progeny regardless of which sex was treated. The dose-response data for RT showed a clear increase with dose for treatment of post-meiotic stages in males and less clear results for treatment of spermatogonia. Oocytes at late follicular stages were resistant to 36-108 rad of x-rays but were very sensitive to higher doses. As to site, 87% of induced tumors were in the lung with the remainder in many other sites. To confirm that the induced tumors were heritable, after initial treatment of only the male parent, the F1 progeny of treated parents were mated and their progeny examined. Besides treatment with RT and U, some mice were treated with 4-nitroquinoline 1-oxide. The induced tumors were inherited as if they were dominant mutations with about 40% penetrance. (12 Refs)

### 7. ENHANCEMENT OF SKIN TUMORIGENESIS BY CIGARETTE SMOKE CONDENSATE FOLLOWING BETA-IRRADIATION IN RATS.

**McGregor JF, Myers DK**
**(c/o Myers) Radiation Biology Branch, Health Sciences Div., Atomic Energy Canada Limited, Chalk River Nuclear Lab., Chalk River, Ontario K0J 1J0, Canada**
**JNCI; 68(4):605-611 1982**

The tumor-promoting ability of cigarette-smoke condensate (CSC) has been demonstrated in rat skin after beta-irradiation. Skin tumors from male albino Charles River CD rats (outbred Sprague-Dawley descended) were classified into two groups: carcinomas and other noncarcinoma tumors. A statistically significant increase (p less than 0.01) in tumor yield occurred after CSC treatment that began 2 mo after irradiation. This finding confirmed our previously published pilot observation. Extension of the pilot experiment to obtain data on carcinoma yield and an experiment to observe the effects of CSC treatment beginning immediately after irradiation were performed. When CSC treatment began immediately after irradiation, the yield of noncarcinoma tumors was significantly reduced (p less than 0.01), whereas the carcinoma yield increased but statistically not significantly (p = 0.12). The increased yield of noncarcinoma tumors is attributed to a significant increase (p less than 0.01) of acute ulceration caused by CSC on recently irradiated skin. The increase in carcinoma yield resulted from an increase in the rate of conversion of noncarcinoma tumors to cancer. Carcinoma yield was also increased by CSC treatment beginning 2 mo after irradiation, but the increase was not significant (p = 0.08). The lack of statistical significance for the carcinoma yields in both experiments may be ascribed to the insufficient number of cancers produced by the treatments. The relative ratios of cancer yields (1.7 and 2.5) did not differ greatly from the 2.2 ratio for the increase of noncarcinoma tumors. The possible relevance of the findings to human carcinogenesis is discussed. (Author abstract) (38 Refs)

### 8. INFLUENCES OF AGE AND ANATOMICAL SITE ON ULTRAVIOLET CARCINOGENESIS IN BALB/C MICE.

**Ebbesen P, Kripke ML**
**(c/o Kripke) Cancer Biology Program, NCI-Frederick Cancer Res. Facility, P.O. Box B, Frederick, MD, 21701**
**JNCI; 68(4):691-694 1982**

Young adult BALB/c mice were more susceptible to the induction of skin tumors from FS40 sunlamps than were 18-mo-old animals. The relative contributions of tissue and host factors to this difference in susceptibility to carcinogenesis were analyzed by reciprocal grafting of skin between young and old animals, followed by repeated exposures of the grafts to UV radiation. More tumors developed in ear skin grafted to the middorsum of young recipients than in that of old recipients, regardless of the age of the skin donor. These ear skin grafts were more susceptible to tumor induction that were comparable grafts of back skin. When large areas of dorsal skin (16 cm2) were grafted to young adult mice, very old skin (greater than 2 yr) was more susceptible to tumor induction than skin that was 1 yr old at the start of irradiation. (Author abstract) (13 Refs)

## EXPERIMENTAL RADIATION MUTAGENESIS

### 9. X-RAY INDUCTION OF PERSISTENT HYPERSENSITIVITY TO MUTATION.

**Frank JP, Williams JR**
**Dept. Radiology, George Washington Univ. Sch. Medicine and Health Sciences, Washington, DC, 20037**
**Science; 216(4543):307-308 1982**

The progeny of x-irradiated V79 cells are hypersensitive to PUVA-(8-methoxypsoralen plus longwave ultraviolet light) induced mutation at the locus for hypoxanthine-guanine phosphoribosyl transferase. This hypersensitivity is most evident at low doses of PUVA that do not induce mutation in non-x-irradiated cells. The hypersensitivity is evoked by x-irradiation delivered as a single dose or as multiple fractions over a long period and persists for at least 108 days of exponential growth. This radiation-induced hypersensitivity to subsequent mutation is a new phenomenon that may be relevant to multistage carcinogenesis. (Author abstract) (8 Refs)

### 10. CLONED TRUNCATED RECA GENES IN E. COLI. I. EFFECT ON RADIOSENSITIVITY AND RECA+ DEPENDENT PROCESSES.

**Sedgwick SG, Yarranton GT**
**Genetics Div., Natl. Inst. Medical Res., London NW7 1AA, England**
**MGG; 185(1):93-98 1982**

Plasmids pMH1 and pDR1461, possessing the control region and 22% or 73% of the Escherichia coli recA gene, conferred UV sensitivity to wild-type uvrA, and umuC bacteria. Sensitization was less in recA441 (tif-1) mutants and absent in lexA cells. Radiosensitization correlated with inhibition of recombinational repair, even through induced recA protein synthesis and recombination in Hfr matings were normal. Plasmids pMH1 and pDR1461 also prevented induction of some, but not all, SOS functions. Mutagenic reversion to tryptophan prototrophy and induced reactivation of UV-irradiated phage lambda were eliminated, and the efficiency of lambda lysogenic induction reduced. However, naladixic acid induced filamentous growth, mitomycin-C induced uvrA gene expression and post UV-irradiation DNA degradation control were little changed. Explanations of these effects are discussed which involve the presence of either truncated recA protein or multiple copies of the recA gene control sequence. (Author abstract) (41 Refs)

### 11. CLONED TRUNCATED RECA GENES IN E. COLI. II. EFFECTS OF TRUNCATED GENE PRODUCTS ON IN VIVO RECA+ PROTEIN ACTIVITY.

**Yarranton GT, Sedgwick SG**
**Genetics Div., Natl. Inst. Medical Res., London NW7 1AA, England**
**MGG; 185(1):99-104 1982**

The ability of plasmids carrying truncated recA genes to sensitize recA+ cells to UV-irradiation was dependent upon the size of the cloned recA gene fragment. Radiosensitization correlated with the inhibition of recombinational repair, and the in vivo reduction of recA protein recombinase activity, as measured by lambdabio11 plating efficiency. W-reactivation was also abolished by the radiosensitizing plasmids, while DNA degradation control, naladixic acid induced filamentation and lambda induction were unaffected. UV-induced mutagenesis in excision proficient Escherichia coli was unaffected, while excision deficient strains were hypermutable. It is suggested that these effects of plasmids bearing 22% or more of the recA gene are the result of the interaction of full-sized and truncated protein subunits to generate multimers unable to catalyze recombination. (Author abstract) (14 Refs)

## EFFECTS OF IRRADIATION ON CHROMOSOMES AND DNA

### 12. X-RAY, UV AND CHEMICAL MUTAGEN SENSITIVITIES OF SKIN FIBROBLASTS FROM PATIENTS WITH FAMILIAL AND CHROMOSOME 13Q-RETINOBLASTOMAS.

**Fujiwara Y, Miyazaki N, Kano Y, Takahashi T, Kaneko A**
**Dept. Radiation Biophysics, Kobe Univ. Sch. Medicine, Kusunoki-cho 7-5-1, Chuo-ku, Kobe 650, Japan**
**J Radiat Res (Tokyo); 22(4):472-476 1981**

The sensitivities of human retinoblastoma (RB) fibroblast strains (AGG1142, RB1JTO, RB1KO) and reference strains NHSF6, NHSF46, and NHSF63 to killing by 170 kVp x-rays, 254 nanometer (nm) UV light, methyl methanesulfonate (mms), monofunctional decarbamoyl mitomycin C (DMC), and bifunctional mitomycin C were tested. The RB strains displayed radiation and mutagen survival curves that were in general similar, and fell within the normal range, as measured by the response of the three NHSF strains. These results strongly suggest that AG1142 cells can repair various types of DNA damage induced by the radiation and cross-linking agents. A 3 to 4-fold increase in sensitivity of RB1JTO (13q-) and RB1KO cells to MMS killing, and a 2-fold higher susceptibility of RB1JTO cells to a UV-type agent (DMC), but not to 254 nm UV was observed, suggesting that MMS and DMC sensitivities may not be universal throughout the RB strains studied. The hypothesis that a specific region on 13q14 may be associated with a presumptive x-ray repair locus governing x-ray sensitivity in an intimate relation to the incidence of RB and second tumors is not supported. (15 Refs)

### 13. GENETIC HETEROGENEITY IN ATAXIA-TELANGIECTASIA STUDIED BY CELL FUSION.

**Jaspers NG, Bootsma D**
**Lab. Cell Biology and Genetics, Erasmus Univ. Rotterdam, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands**
**Proc Natl Acad Sci USA; 79(8,part1):2641-2644 1982**

The effect of x-rays on the rate of semiconservative DNA replication was investigated by autoradiography in single cells obtained from normal individuals and from patients having ataxia-telangiectasia (AT). In the five AT cell strains studied, the rate of DNA synthesis was inhibited to a lesser extent than in two normal cell strains. By using this abnormal regulation of DNA replication in AT cells as a marker, an experimental procedure was developed that allowed genetic complementation analysis of AT. After Sendai virus-induced fusion of AT cells, the grains were counted over binucleate cells with both nuclei in S phase. In some cases, the inhibition of DNA synthesis caused by x-rays in the heterodikaryons was more pronounced than that in the parental homodikaryons and was comparable to that in normal binucleate cells, indicating complementation. By using this approach, the five AT cell strains that were investigated could be assigned to three complementation groups. The data suggest that extensive genetic heterogeneity exists in AT. (Author abstract) (15 Refs)

### 14. COMPLEMENTATION OF THE DEFECTS IN DNA SYNTHESIS IN IRRADIATED AND UNIRRADIATED ATAXIA-TELANGIECTASIA CELLS.

**Murnane JP, Painter RB**
**Lab. Radiology and Environmental Health, Univ. California, San Francisco, CA, 94143**
**Proc Natl Acad Sci USA; 79(6,part1):1960-1963 1982**

Mutant subtypes in the human genetic disease ataxia-telangiectasia (A-T) were classified by means of an assay system that monitors complementation of defects in DNA synthesis. Anomalies in DNA synthesis have been observed previously in A-T cells, both in their failure to inhibit DNA synthesis immediately after exposure to ionizing radiation and in their prolonged S phase. Polyethylene glycol-mediated cell fusion and autoradiography were combined with selective identification of different A-T cell populations by fluorescent colored microspheres to determine complementation capabilities of various A-T cell combinations. Five complementation groups were identified by both a 30-40% increase in the rate of DNA synthesis in unirradiated heterokaryons and the appearance of normal inhibition of DNA synthesis after x-irradiation of heterokaryons.

The correlation observed between these phenomena suggests that the defects in A-T cells involve problems in initiation of DNA synthesis. (Author abstract) (20 Refs)

### 15. HETEROGENEOUS RESPONSE TO X-RAY AND ULTRAVIOLET LIGHT IRRADIATIONS OF CULTURED SKIN FIBROBLASTS IN TWO FAMILIES WITH GARDNER'S SYNDROME.

**Kinsella TJ, Little JB, Nove J, Weichselbaum RR, Li FP, Meyer RJ, Marchetto DJ, Patterson WB**
**Radiation Oncology Branch, Div. Cancer Treatment, NCI, NIH, Building 10, Room B3-B38, Bethesda, MD, 20205**
**JNCI; 68(5):697-701 1982**

A heterogeneous response to x-ray and far UV (254 nm) light irradiations was found in cultured skin fibroblast lines from two separate families with Gardner's syndrome. When compared to two normal control cultures and cultures from two patients with nonfamilial colon cancer, cultures from four clinically affected members of Family 1 showed increased sensitivity to the lethal effects of both x-ray and UV light irradiations. These cell lines also showed a delayed pattern of x-ray potentially lethal damage repair (PLDR) and absent UV PLDR. In contrast, cultures from three members of Family 2 (2 of whom were clinically affected) showed a normal response of survival and PLDR to both x-ray and UV light irradiations. Thus increased sensitivity of cultured skin fibroblasts to x-ray and UV light irradiations was not a consistent in vitro finding in patients with Gardner's syndrome. However, in families with Gardner's syndrome who demonstrate in vitro radiosensitivity, additional studies are needed to assess the usefulness of these techniques in detecting affected individuals prior to the development of colon carcinoma and other manifestations. (Author abstract) (29 Refs)

### 16. ELEVATED SISTER CHROMATID EXCHANGE (SCE) RATE IN PATIENTS WITH SUN-INDUCED SKIN TUMORS.

**Jung EG, Luchsinger P, Bohnert F**
**Dept. Dermatology, Faculty Clinical Medicine at Mannheim, Univ. Heidelberg, P.O. Box 23, D-6800 Mannheim, W. Germany**
**Arch Dermatol Res; 272(1/2):151-153 1982**

Effects of the spontaneous sister chromatid exchange (SCE) and the UV C rays (UVC)-induced increase of SCE in peripheral leukocytes on the risk for actinic keratosis and sun-induced malignancies were studied. SCE with and without UVC irradiation was studied in vitro in peripheral leukocytes of 21 patients with sun-induced, non-melanoma skin tumors (actinic keratoses, basal cell and prickle cell carcinomatas) and compared with a control group of 21 healthy volunteers of the same age (30-75 yr old). The mean values and the standard deviations are shown. In the non-melanoma tumor group the spontaneous SCE and the light-stimulated increase of the phenomenon is significantly higher than in the melanoma group. SCE is currently being used to determine spontaneous and induced mutagenic and carcinogenic effects on chromosomes and cells. SCE are positively correlated with the mutation rate and are compatible with the cell survival. The higher SCE in patients with sun-induced non-melanoma skin tumors evidences an elevated somatic mutagenicity in leukocytes and rises the question whether this is an additional risk factor, completing the risk spectrum to be established. Non-melanoma and melanoma groups behave differently regarding the degree of SCE elevation and DNA repair activity in leukocytes. (8 Refs)

### 17. RADIATION-INDUCED CHROMOSOME ABERRATIONS IN LYMPHOCYTES FROM MAN AND CRAB-EATING MONKEY. THE DOSE-RESPONSE RELATIONSHIPS AT LOW DOSES.

**Takahashi E, Hirai M. Tobari I, Utsugi T, Nakai S**
**Div. Genetics, Natl Inst. Radiological Sciences, 9-1, 4-Anagawa, Chiba 260, Japan**
**Mutat Res; 94(1):115-123 1982**

The dose-response relationship (DRR) at low-dose irradiation levels (5-50 rad) was examined to find out whether DRR was fitted to the linear-quadratic (LQ) model by using peripheral lymphocytes from man and monkey, and to investigate the difference in dose-response curves regarding the yields of chromosome aberrations (CAB), especially dicentrics, between man and monkey. Heparinized peripheral whole blood from a healthy 29-yr-old human male and from a 5-yr-old male crab-eating monkey (Macaca fascicularis) was used. As the results obtained from five to six repeated experiments were not significantly different, data for each dose were pooled and are presented. The spontaneous yield of CAB was examined only for the monkey, 16,249 metaphase cells being scored. The spontaneous frequency of dicentrics was estimated to be 0.018 +- 0.011 per 100 cells for the monkey, and 0.009 +-0.006 for human lymphocytes. No statistically significant difference was found in the spontaneous yield of dicentrics between man and monkey. DRR for dicentrics in human lymphocytes obtained from combining data from low-dose with data from high-dose (100-400 rad) experiments is presented. The dicentric yield was fitted better to the LQ model than to the power-law model. For monkey, a similar dose-relationship was calculated. Statistical analysis for the difference between observed and expected yields indicates that the dicentric yield does not fit well either the power-law model or LQ model. Only little difference was found in the yield of acentrics between man and monkey, except at 10 rad. Results showed that the dose-response curves expected from LQ model deviate significantly from linearity at the low-dose level. (19 Refs)

### 18. INDUCTION OF CHROMOSOME DAMAGE BY ULTRAVIOLET LIGHT AND CAFFEINE: CORRELATION OF CYTOGENETIC EVALUATION AND FLOW KARYOTYPE.

**Cremer C, Cremer T, Gray JW**
**Biomedical Sciences Div., Lawrence Livermore Natl. Lab., Livermore, CA, 94550**
**Cytometry; 2(5):287-290 1982**

The flow karyotype (FKT) of Chinese hamster cells after treatment with UV light and caffeine (CF) was investigated and the correlation between the debris in FKT and the frequency of cells with generalized chromosome shattering (GCS) and with chromosome damage were studied. A derivative (650 A) of the M3-1 Chinese hamster cell line was used. The increase in frequency of mitotic cells (MC) showing GCS and other aberrations with increasing UV exposure is presented. The percentage of MC with GCS was very low after CF treatment alone but increased drastically to almost 90% as the UV fluence increased to 7.5 Joule/square meter (J/m2). UV irradiation alone did not induce GCS (%GCS less than 1; % aberrant up to 5) in the dose range investigated. The effect of UV plus CF treatment on FKT is shown. The debris continuum in FKT of UV irradiated cells (5 J/m2) postincubated with CF increased so drastically that no clear chromosome peaks were obtained. The relative debris level in FKT is shown as a function of the UV fluence for cells treated with UV and postincubated with or without CF. While no marked increase in relative debris level was observed following UV irradiation alone or CF treatment alone, the relative debris level was increased strongly with UV fluence after the combined treatment. Microscopic examination of chromosome suspensions revealed a high frequency of chromosome fragments. Whether the observed effects are due to a high number of chromosome breaks existing prior to chromosome isolation or to an increased chromosomal fragility is not known. (22 Refs)

### 19. DNA CONTENT OF CELLS WITH GENERALIZED CHROMOSOME SHATTERING INDUCED BY ULTRAVIOLET LIGHT PLUS CAFFEINE.

**Cremer C, Gray JW**
**Biomedical Sciences Div., Lawrence Livermore Natl. Lab., Univ. California, Livermore, CA, 94550**
**Mutat Res; 94(1):133-142 1982**

The results of flow cytometric analyses of DNA content of UV and caffeine-treated Chinese hamster ovary (CHO) cells are reported. CHO cells growing asynchronously were exposed to 5.0 Joules/square meter UV (254 nanometer) and then incubated with or without 2 milliM caffeine. Very few generalized chromosome shattering (GCS)-cells were observed in control cultures or in cultures treated with UV or caffeine alone. However, the GCSm (number of cells with GCS-like appearance/number of cells with condensed, chromosome-like chromatin x 100) and GCSt (%GCSm x mitotic index) increased sharply to 86 and 10, respectively, after treatment with UV plus caffeine. Fluorescence distributions for control, UV-treated and caffeine-treated cells were very similar. Peak B in fluorescence distributions of UV- and/or caffeine-treated cells corresponded to a normal G2M content. All GCS-like cells were found to have the G2M DNA content. These results suggest a subtle process resulting in failure of normal chromosome condensation after most or all of the DNA has been replicated in GCS-like cells. (29 Refs)

### 20. AN ALKALINE SEPARATION METHOD FOR DETECTION OF SMALL AMOUNT OF DNA DAMAGE.

**Sakai K, Okada S**
**Dept. Radiation Biophysics, Faculty Medicine, Univ. Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113, Japan**
**J Radiat Res (Tokyo); 22(4):415-424 1981**

The alkaline separation method for detection of DNA damage was made quantitative by calibration with an alkaline sucrose gradient centrifugation, and applied to analysis of DNA damage in cultured mouse leukemic L5178Y cells after x-irradiation. The new method can detect DNA damage, probably scissions and alkali-labile sites, but not sinlge- and double-strand breaks. The method can also detect DNA damage due to ethyl methanesulfonate or 4-nitroquinoline 1-oxide. (14 Refs)

### 21. SERIAL ANALYSIS OF CHROMOSOMAL ABERRATIONS AND PROLIFERATION KINETICS OF MOUSE SPERMATOGONIA AFTER SINGLE OR FRACTIONATED X-RAY EXPOSURES.

**Hirai M, Van Buul PP**
**(c/o van Buul) Dept. Radiation Genetics and Chemical Mutagenesis, State Univ. Leiden, Sylvius Labs., Wassenaarseweg 72, 2333 AL Leiden, The Netherlands**
**Mutat Res; 93(2):419-437 1982**

X-ray-induced chromosomal aberrations were studied in dividing spermatogonia of 10-15 wk old male Swiss random-bred (Cpb(SE)S) mice. Single doses of 50, 100, and 150 rad were followed by examination of cytogenetic effects continuously from 4-48 hr after irradiation, together with bromodeoxyuridine (BrdU) labeling of spermatogonial chromosomes in vivo to provide cell kinetics after irradiation. A fractionation experiment was also performed (100 + 50 rad, with 24 hr interval). Chromatid-type aberrations show the highest incidence for all doses at the first fixation times. The peak yield of chromosome-type aberrations occurs at about 24 hr for 50 rad, and about 30 hr for 100 and 150 rad, suggesting 6-8 hr extra mitotic delay for higher exposures. BrdU-labeling suggested an 18-hr delay in cell-cycle progression from 100-and 150-rad treatments; the discrepancy in the two methods may be explained by analysis of the rate of cell killing. A low mitotic activity was observed from 20 to 40 hr, a period of high frequencies of chromosome-type aberrations. The G2 phase is far more sensitive to chromosomal aberration production by x-rays in terms of number of breaks per cell than the G1 or S phases. None of the parameters analyzed, ie, time sequence of chromosomal aberrations, mitotic activity, and cell kinetics, exhibited a threshold effect with respect to x-ray dose, indicating the absence of sensitization. (39 Refs)

### 22. METABOLISM OF NUCLEIC ACIDS IN THE THYMUS OF RATS SUBJECTED TO COMBINED EXPOSURE TO GAMMA-RADIATION AND PLUTONIUM-239.

**Elkina NI**

**No affiliation given**

**Radiobiologiia; 22(1):35-39 1982**

Metabolism of DNA and RNA was studied in the thymus of Wistar rats subjected to external irradiation with 137Cs gamma rays and administration of Plutonium-239. The 1-yr follow-up showed that combined exposure produced more pronounced changes in the thymus wt, cellularity, and in the rate of DNA and RNA biosynthesis than gamma radiation alone. (14 Refs) (In RUS)

## OTHER CELLULAR EFFECTS OF IRRADIATION

### 23. DISTURBANCES IN LYSOSOMAL ENZYME ACTIVITIES IN RATS FOLLOWING EXPERIMENTAL POSTRADIATION DISEASE.

**Drozdz M, Piwowarczyk B, Olczyk K, Pikula-Zachara M**

**Zaklad Chemii Klinicznej, Instytut Farmakodynamiki i Analytiki Medycznej Sl. Am., ul. Borowkowa 24, 40-692 Katowice, Poland**

**Med Pr; 32(3):201-206 1981**

The effect of irradiation (500 rads) on lysosomal enzyme activities in serum, leukocytes, liver, kidneys, lungs, and heart of 6-mo-old male Wistar rats was studied 30 days after irradiation. The increased acid phosphatase (AP), beta-glucuronidase and beta-acetylglucosaminidase activities in the tissues were indicative of the labilizing effect of irradiation on lysosomal membranes. Kidneys, lungs and liver were found to be the most radiosensitive organs. The AP activity showed the greatest increase in serum and leukocytes. The activities of all enzymes examined were reduced in hepatic lysosomes. (55 Refs) (In POL)

## THEORETICAL ASPECTS OF RADIATION CARCINOGENESIS

### 24. THE ESTIMATION OF LOW-DOSE HAZARDS BY EXTRAPOLATION FROM HIGH DOSES.

**Rossi HH**
**Radiological Res. Lab., Columbia Univ., 630 West 168th St., New York, NY, 10032**
**Yale J Biol Med; 54(5):339-344 1981**

Empirical information on the effects of low doses of ionizing radiation is beset by severe limitations. Theoretical considerations of biophysics can guide the analysis of epidemiological data by indicating certain dose-response relations or eliminating others. Thus, it can be shown that at low doses there must be proportionality between dose and effect on non-interacting cells and that one must anticipate different dose-effect relations upon exposure to markedly different types of radiation. (Author abstract) (10 Refs)

### 25. STATISTICAL LIMITATIONS IN RELATION TO SAMPLE SIZE.

**Land CE**
**Environmental Epidemiology Branch, NCI, Bethesda, MD, 20205**
**Environ Health Perspect; 42:15-21 1981**

Examples from radiation carcinogenesis are used to illustrate difficulties in estimating cancer risks for low doses of a carcinogen. Using direct estimation based on data from a population exposed to low doses, an example is given for a linear dose-response relationship for female breast cancer induced by exposure to sparsely ionizing radiation. Leukemia incidence data from a life span study of Nagasaki A-bomb survivors is used to illustrate curve fitting, by which higher dose data determine lower risk estimates. Although more is known about dose-response relationships for ionizing radiation than for any other environmental carcinogen, estimates of cancer risk for low radiation doses have sometimes disagreed by factors of 100 or more. (11 Refs)

### 26. EXPLORATION FROM INCOMPLETE DATA TO TOTAL OR LIFETIME RISKS AT LOW DOSES.

**Schneiderman MA**
**Clement Associates, Inc., 1010 Wisconsin Ave., N.W., Washington, DC, 20007**
**Environ Health Perspect; 42:33-38 1981**

Estimation of human risk from exposure to carcinogens is discussed; risk estimation is based both on epidemiology and laboratory data. In chronic disease epidemiology, data is gathered for both nonpositive and positive occupational cancer studies; the Occupational Safety and Health Administration has laid out rigid standards pertaining to these studies, but often, epidemiologic data cannot conform to these standards. Examples from radiation carcinogenesis are used to challenge traditional dose response relationships. Existing data may be inadequate for extrapolation to humans in any detail or for application to specific population subgroups. (12 Refs)

### 27. GAMMA-RAY INDUCED LUNG ADENOCARCINOMA IN THE MOUSE.

**Rosen P**
**Hasbrouck Lab., Univ. Massachusetts, Amherst, MA, 01003**
**Med Hypotheses; 8(3):297-301 1982**

A model of carcinogenesis in which the operator region of the operon controlling mitosis is damaged by a carcinogenic agent and subsequently sustains a mutation is discussed. A theoretical calculation of gamma-ray induced adenocarcinoma of mouse lung at low dose rates was performed. From this calculation the fraction of nascent neoplastic cells not escaping the immune surveillance was calculated. For doses from 0-200 rad the fraction is approx twice the value for humans which is approx 1/25. (17 Refs)

### 28. MOLECULAR EVENTS BASIC TO CELLULAR RADIATION RESPONSE.

**Kolodny GM**
**Radiology Res. Lab., Massachusettes General Hosp., Boston, MA**
**Aerosp Med Biol; (229):14 1982**

The initiation and control of the division process in normal cells to gain insight into changes caused by x-irradiation and neoplasia were discussed. It is suggested that small mol wt RNA acts as primer for new RNA synthesis by hybridizing with DNA and there initiating the transcription of a new RNA chain. It is indicated that small mol wt RNA induce the production of new protein. It is demonstrated that RNA is taken up from the media by cells in culture and induce in vitro the production of differential cell products. (Author abstract)

### 29. ESTIMATION OF THE CONTRIBUTION OF IONIZATION AND EXCITATION TO THE LETHAL EFFECT OF IONIZING RADIATION.

**Petin VG, Komarov VP**
**Biophysical Lab., Res. Inst. Medical Radiology, USSR Acad. Medical Sciences, Obninsk, USSR**
**Radiat Environ Biophys; 20(2):79-87 1982**

A theoretical model is developed for estimating the relative contributions of ionization and excitation of DNA to the lethal effect of ionizing radiation. Studies of the photoreactivation of UV induced damage to Escherichia coli are analyzed in terms of this model. The data are consistent with the hypothesis that the UV component of Cerenkov radiation plays a role in the formation of excitations responsible for the lethal effect and for the phenomenon of photoreactivation after ionizing radiation. (24 Refs)

## ENVIRONMENTAL RADIATION AND PROTECTION STANDARDS

### 30. CELLULAR LUNG DOSIMETRY FOR INHALED RADON DECAY PRODUCTS AS A BASE FOR RADIATION-INDUCED LUNG CANCER RISK ASSESSMENT: I. CALCULATION OF MEAN CELLULAR DOSES.

**Hofmann W**
**Abteilung fur Biophysik am Institut fur Allgemeine, Biologie, Biochemie und Biophysik Universitat Salzburg, A-5020 Salzburg, Austria**
**Radiat Environ Biophys; 20(2):95-112 1982**

Deposition and retention calculations for inhalation of Rn222 and its decay products are presented as a base for cellular dosimetry in different lung regions. The influence of various environmental and personal factors (dosage, age, respiratory minute volume, aerosol characteristics, mucociliary clearance, humidity, and inter- and intraindividual variability) on the cellular dose distribution is discussed. (46 Refs)

## 31. CELLULAR LUNG DOSIMETRY FOR INHALED RADON DECAY PRODUCTS AS A BASE FOR RADIATION-INDUCED LUNG CANCER RISK ASSESSMENT: II. MICRODOSIMETRIC CALCULATIONS.

**Hofmann W**
**Abteilung fur Biophysik am Institut fur Allgemeine, Biologie, Biochemie und Biophysik Universitat Salzburg, A-5020 Salzburg, Austria**
**Radiat Environ Biophys; 20(2):113-122 1982**

An image analysis-aided microdosimetric model has been developed and used to estimate specific energy probability distributions in rat lung cells. Homogeneous and hot spot nuclide distributions are compared. Results obtained for rat lung are extrapolated to the human lung. Statistical variations of energy imparted in microscopical sites are discussed. Single event density distributions together with the number of cells receiving single hits appear to represent more appropriate parameters than mean radiation doses. (12 Refs)

## 32. AN EVALUATION OF WORKING LEVEL MEASUREMENTS USING A GENERALIZED KUSNETZ METHOD.

**Borak TB, Franco ED, Holub RF**
**Dept. Radiology and Radiation Biology, Colorado State Univ., Fort Collins, CO, 80523**
**Health Phys; 42(4):459-467 1982**

A systematic procedure for evaluating inherent error and precision is presented for methods which determine Working Level from a single measurement of alpha activity. Optimized conversion factors are given for typical conditions encountered in uranium mines. Symmetries involving sampling and counting intervals are described. The evaluation scheme is then used to examine uncertainties in measurements of very small values of Working Level anticipated in buildings and houses. (Author abstract) (24 Refs)

## 33. RADON AND THORON DAUGHTERS IN HOUSING.

**Gunning C, Scott AG**
**DSMA/ACRES, 4195 Dundas St. West, Toronto, Ontario M8X 1Y4, Canada**
**Health Phys; 42(4):527-528 1982**

Radon and thoron daughter concentrations in housing expressed in Working Levels (WL) were estimated by a modified Kusnetz technique (2 alpha counts) in a region containing uranium mines. The air filter samples were taken each morning in house basements as part of the routine survey. A total of 174 filters from 95 different houses were evaluated during 1 mo. House windows were closed when the samples were taken. Results indicate that the WL for thoron daughters in houses is insignificant compared with the WL for radon and its remedial action limit of 20 milliWL. (2 Refs)

## 34. RADON DAUGHTER EXPOSURE TO URANIUM MINERS.

**Cohen BL**
**Univ. Pittsburgh, Pittsburgh, PA, 15213**
**Health Phys; 42(4):449-457 1982**

Radon exposures to US uranium miners under present conditions average about 1.3 WLM per yr approx 60 WLM per full working lifetime. This is intermediate between (a) the lowest exposures for which there have been excess lung cancers reported among US miners (120-240 WLM) and (b) average environmental radon exposures (16 WLM), so models based on these two situations are used to estimate expected effects on present uranium miners. In Model A, the loss of life expectancy is 45 days, the SMR (standardized mortality ratio) for lung cancers is 1.10, and the SMR for all causes between ages 18 and 65 is 1.013. In Model B there are 10 days, 1.03 and 1.002 respectively. It is shown that the radon exposures to miners are similar to those to millions of Americans from environmental exposure, and that miner health risks are comparable to those of other radiation workers. Their lung cancer risk from radon is 7-50 times less than their job-related accident mortality risk, and represents 0.7-4% of their total risk in mining. Miners suffer from many diseases with SMR very much larger than that for radon-induced lung cancer, and there are many other occupations and industries with far higher SMR for lung cancer than that from radon exposure to miners. (Author abstract) (20 Refs)

## 35. RADON DAUGHTER EQUILIBRIUM AND UNATTACHED FRACTION IN MINE ATMOSPHERES.

**Stranden E, Berteig L**
**State Inst. Radiation Hygiene, Osterndalen 25, 1345 Osteras, Norway**
**Health Phys; 42(4):479-487 1982**

Measurements of the equilibrium between radon and its daughters in mine atmospheres are presented. The situation in mines seems to be too complex to be described by any simple theoretical model. There is however a good correlation between the equilibrium factor, F, and the individual daughter ratios. This suggests that the individual daughter concentrations may be assessed by Kusnetz-measurements of the equilibrium factor, F. Measurements by the wire screen method indicate that the dust concentration is the main influencing factor upon the unattached fraction of the radon daughters. The unattached fraction of the potential alpha-energy was lower than 0.05 in most mining situations. In areas with very clean air, the unattached fraction may however be higher than 0.3. Measurement indicated a good correlation between the unattached fraction of the potential alpha-energy and the unattached fraction of the individual daughter products. This suggests that assessments of the unattached fraction of the individual daughters may be obtained by using the Kusnetz method for measurements on the screen and back up filter. (Author abstract) (11 Refs)

## 36. CONCENTRATION 239,240 PU IN HUMAN AUTOPSY TISSUES. PRELIMINARY REPORT OF A COMPARATIVE STUDY ON DIFFERENT POPULATIONS.

**Kawamura H, Tanaka G, McInroy JF, Eutsler BC**
**Div. Radioecology, Natl. Inst. Radiological Sciences, 3609 Isozaki, Nakaminato-shi, 311-12, Japan**
**J Radiat Res (Tokyo); 22(4):373-380 1981**

Concentrations of 239,240Pu were studied in autopsy material of males and females (21-69 yr old) who died in Tokyo in 1970. Lung and liver specimens were obtained from 10 subjects; kidney samples were also obtained from five. Bone samples were obtained from another 10 subjects, including some of the above. Tissue ash samples were analyzed for 239,240 Pu content by a radiochemical procedure and the alpha spectrometric method developed at the Los Alamos National Laboratory. Data obtained from the Japanese subjects' tissues were compared with similar data from the Los Alamos data base for 1970 autopsy cases from the United States. Lung, liver, and kidney 239,240 Pu concentrations in the Japanese population were significantly lower than in the United States populations, whereas concentration of 239,240 Pu in vertebra was significantly higher in Japan. Bovine liver and kidney samples from

Japan showed no measurable concentration of 239,240 Pu. The discrepancies in values between the United States and Japan indicate the need for further studies of concentration of Pu and other transuranic elements in human tissues. (16 Refs)

### 37. 137CS CONCENTRATIONS IN NORTHERN ALASKAN ESKIMOS, 1962-79: EFFECTS OF ECOLOGICAL, CULTURAL AND POLITICAL FACTORS.

**Hanson WC**
**Ertec Northwest, Inc., 420 L St., Suite 406, Anchorage, AK, 99501**
**Health Phys; 42(4):433-447 1982**

Concentrations of worldwide fallout 137Cs were measured in the lichen-caribou-Eskimo food chain of northern Alaska during the period 1962-79. Pronounced inputs of fallout occurred after major nuclear weapons tests in the atmosphere and 137Cs was transmitted through the food chain to Eskimos with about a 2-yr delay due to environmental parameters. Caribou (Rangifer tarandus) meat sampled during spring harvest contained 4 times the 137Cs concentration of lichens obtained from their winter range. Calculated caribou meat ingestion rates of Anaktuvuk Pass Eskimos during winter ranged from approx 1 kg/day in 1964 to 0.16 kg/day in 1977. Several environmental factors affected seasonal patterns and amounts of 137Cs transferred through the food chain. Maximum 137Cs concentrations of approx 20 nCi/kg body wt in Eskimos occurred in 1964 and have now decreased to approx 0.5 nCi/kg, largely because of cultural and political factors. Radiation doses from 137Cs body burdens during the study period ranged from 60 mrad/yr in 1962 to approx 140 mrad/yr during the 1962-64 maxima and decreased to 8 mrad/yr in 1979. (Author abstract) (62 Refs)

### 38. THE ICRP DOSE LIMITATION SYSTEM - SOLUTION OR PROBLEM?

**Healy JW**
**Los Alamos Natl. Lab., P.O. Box 1663, Los Alamos, NM, 87545**
**Health Phys; 42(4):407-415 1982**

The dose limitation system of the ICRP is examined in relation to internal emitters. It is noted that the risk for many radionuclides is not equivalent to that of an external, whole-body dose equivalent of 5 rem/yr because of the imposition of the non-stochastic limit. For other radionuclides the risk is limited by the choice of weighing factors. Problems and uncertainties in the use of the system are discussed and the conclusion is reached that it should not be adopted in the US. (Author abstract) (15 Refs)

### 39. EFFECT OF POLYMERIC PLUTONIUM ON THE HEMATOPOIETIC ACTIVITY IN THE BONE MARROW OF MICE.

**Joshima H, Kashima M, Enomoto H, Matsuoka O**
**Div. Radiation Hazards, Natl. Inst. Radiological Sciences, Anagawa, Chiba 260, Japan**
**J Radiat Res (Tokyo); 22(4):425-433 1981**

Changes in the numbers of nucleated cells and in vivo colony forming units (CFUs) in the femoral marrow of 14-wk-old CF 1/Nrs mice after injection of varied doses of polymeric plutonium (1.67 uCi 239 Pu/ml), blood clearance of 59Fe, 59Fe incorporation into circulating erythrocytes, and tissue distribution of 59Fe were studied. The number of nucleated cells decreased in proportion to the amount of plutonium injected. The number of CFUs per 10(5) nucleated cells was significantly reduced only at 56 days after injection of 10 and 15 uCi/kg of 239Pu, indicating that a fairly large dose of radiation is necessary to reduce CFUs. Incorporation of 59Fe into circulating erythrocytes was reduced after injection of plutonium. Increased hepatic uptake of 59Fe was observed at 56 days after injection of the highest dose. 59Fe uptake into the spleen was smallest at intermediate doses of plutonium. The hematological activity of the bone marrow evidently is disturbed by a dose of 239Pu as low as 5 uCi/kg, with which clinically detectable anemia is not induced. (14 Refs)

### 40. PROBLEMS IN EVALUATING RADIATION DOSE VIA TERRESTRIAL AND AQUATIC PATHWAYS.

**Vaughan BE, Soldat JK, Schreckhise RG, Watson EC, McKenzie DH**

**Ecological Sciences Dept., Pacific Northwest Lab., Battelle Memorial Inst., Richland, WA, 99352**

**Environ Health Perspect; 42:149-161 1981**

Environmental pathways models used for predictive assessment of radiation dose are discussed and characteristics of mathematical exposure models are described. Detailed evaluations are made of source considerations influencing dose, including dispersal mechanisms, mobilization and uptake mechanisms, and critical food pathways. Accuracy of dose estimates is usually overestimated in practice from two to six times due to the use of generic concentration ratios instead of site specific data. The need to improve parametrization of pathways models so as to increase validity is discussed. (73 Refs)

### 41. UNEXPECTED 226RA BUILD-UP IN WET-PROCESS PHOSPHORIC-ACID PLANTS.

**Lardinoye MH, Weterings K, Van de Berg WB**

**(c/o Weterings), Central Lab., DSM P.O. Box 18, 6160 MD Geleen, The Netherlands**

**Health Phys; 42(4):503-514 1982**

During an investigation of the distribution or radium and uranium over the different process streams in phosphoric-acid production and in the nitrophosphate route, a higher than average radiation level was detected in the vicinity of some piping and vessels near the gypsum filters. This higher radiation level is caused by radium, which, as a decay product in the 238U series, is present in very low concentrations (1-50 pCi 226R/g) in the phosphates used for fertilizer production. Specific research later on established that there were detectable radiation levels around vessels and piping in other phosphoric-acid works as well. It turned out that in all factories the filter part, and especially the washing-acid section showed the highest radiation-level. In the piping of the gypsum filter, through which the washing acid is discharged, a scaling of barium sulfate and calcium sulfate with a higher radium concentration (+-0.1 Ci/g) is formed. The radium ions appeared to be incorporated in the barium sulfate lattice, hence the solubility of the radium precipitate is very low. The danger of internal pollution, for example in cleaning operations by radio-active intake or inhalation of radon is very small in the cases described. The risk of external radiation can be prevented by periodically cleaning (every 1-3 yr) the equipment in which the radio-active scaling is formed. (Author abstract) (5 Refs)

### 42. COMPARISON OF PHYSICAL CHEMICAL PROPERTIES OF POWDERS AND RESPIRABLE AEROSOLS OF INDUSTRIAL MIXED URANIUM AND PLUTONIUM OXIDE FUELS.

**Eidson AF**
**Inhalation Toxicology Res. Inst., Lovelace Biomedical and Environmental Res. Inst., P.O. Box 5890, Albuquerque, NM, 87185**
**Health Phys; 42(4):531-536 1982**

Physical and chemical properties that may be important in determining the metabolism of accidentally released, inhaled aerosols were characterized and the properties of bulk powders and the respirable fraction they include were compared. The studies were a part of a program to relate physical and chemical properties of respirable aerosols to the subsequent distribution of radiation dose in tissues of laboratory animals exposed to these aerosols by inhalation. Analysis of mixed uranium and plutonium oxide aerosols inhaled by fuel fabrication workers is discussed. (19 Refs)

### 43. DISSOLUTION FRACTIONS AND HALF-TIMES OF SINGLE SOURCE YELLOWCAKE IN SIMULATED LUNG FLUIDS.

**Dennis NA, Blauer HM, Kent JE**
**Office Nuclear Regulatory Res., United States Nuclear Regulatory Commission, Washington, DC, 20555**
**Health Phys; 42(4):469-477 1982**

Thirty-five samples of yellowcake, the primary product of uranium milling, were obtained from industry. Samples were selected from the archives of 6 yr of yellowcake production from a single uranium milling operation. Ten representative samples were selected on the basis of color variation and chemical composition. Dissolution fractions and half-times were obtained using both simulated interstitial and simulated surfactant lung fluids maintained in vials submerged in a shaker water bath at 37 C for 26 days. Samples were collected at 12 different time intervals and fresh simulant replaced. Uranium concentrations were analyzed by fluorometric methods using ASTM techniques. The fraction of the uranium undissolved, F, can be well modeled by the sum of three exponential terms. Dissolution fractions and half-times in the two simulated lung fluids were found to be not significantly different. The final characterization of yellowcake resulting from this investigation strongly suggests that dissolution rates of yellowcake from a single source may be individually process specific or site specific. (18 Refs)

## REVIEWS AND OTHER STUDIES

### 44. LIMITATIONS AND PROBLEMS IN DERIVING RISK ESTIMATES FOR LOW-LEVEL RADIATION EXPOSURE.

**Cohen BI**
**Dept. Physics, Univ. Pittsburgh, Pittsburgh, PA, 15260**
**Yale J Biol Med; 54(5):329-338 1981**

Some of the problems in determining the cancer risk of low-level radiation from studies of exposed groups are reviewed and applied to the study of Hanford workers by Mancuso, Stewart, and Kneale. Problems considered are statistical limitations, variation of cancer rates with geography and race, the 'healthy worker effect', calendar yr and age variation of cancer mortality, choosing from long lists, use of proportional mortality rates, cigarette smoking-cancer correlations, use of averages to represent data distributions, ignoring other data, and correlations between radiation exposure and other factors that may cause cancer. The current status of studies of the Hanford workers is reviewed. (Author abstract) (37 Refs)

### 45. CHROMOSOMAL METHODS IN POPULATION STUDIES.

**Conner MK, Wald N**
**Graduate Sch. Public Health, Univ. Pittsburgh, Pittsburgh, PA, 15262**
**Environ Health Perspect; 42:107-113 1981**

Chromosomal aberrations and sister chromatid exchanges (SCE) are described as a means for evaluating DNA damaging agents. Biological changes produced by low level radiation exposure may be detected with sensitivity, using cytogenetic aberration scoring of human blood cells. Examples of in vivo cytogenetic studies of low level radiated populations are tabulated. Adequate sample size requirements and accurate assessment of cumulative exposure effects with increased age are important for reliable cost benefit analysis of low level exposure. Implications of SCE for an individual's health or for the general public's genetic health is discussed. (40 Refs)

### 46. PUVA: GAMBLING WITH A SYSTEM.

**Strauss GH**
**EPA, MD 68, Research Triangle Park, NC, 27711**
**Int J Dermatol; 21(3):136-137 1982**

Evidence for the pseudo-promoter (permissive carcinogen) status of psoralen-ultraviolet A (PUVA) is reviewed in regard to treatment of psoriasis. Xeroderma pigmentosum patients treated with PUVA have developed multiple cutaneous neoplasms within 1 mo. Other patients at risk for skin cancer have developed in less than 3 yr after PUVA therapy. Because PUVA suppresses delayed cellular hypersensitivity (DCH), patients undergoing PUVA therapy, particularly those with light skin getting intensive treatment, should be monitored for DCH response to dinitrochlorobenzene. (8 Refs)

### 47. SOME ASPECTS OF CANCER EPIDEMIOLOGY.

**Lilienfeld AM**
**Sch. Hygiene and Public Health, Johns Hopkins Univ., 615 N. Wolfe St., Baltimore, MD, 21205**
**Biometrics; 38(Suppl):155-160 1982**

Epidemiologic studies have strongly suggested that a vast majority (80-90%) of cancers are caused by radiation, chemical and biologic agents; the remainder result from endogenous or genetic factors. Biologically, cancer is most probably the end result of a complex multistage process and therefore may be due to a sequence of exposures to different agents at each of these stages. This emphasizes the need to stress the study of interactions in epidemiologic studies to a greater extent than has been done thus far. Examples of the importance of interactions in several types of cancer are presented. (Author abstract) (8 Refs)

### 48. RELATIONSHIP BETWEEN VITAMIN E AND CANCER - FACTS, NOT FANCY.

**Ellison NM**
**Dept. Medical Oncology, Geisinger Medical Center, Danville, PA**
**Cancer Bull; 34(1):43-44 1982**

The roles of vitamin E in inhibition of carcinogenesis and amelioration of conventional cancer treatment toxicity are discussed. Studies with mammalian models suggest that vitamin E may act as a protector against radiation-induced cellular damage and as a radiosensitizer in cancer treatment. The conflict between these antagonistic functions must be resolved. Vitamin E has been shown to ameliorate the toxic effects of doxorubicin in animal models without adversely affecting antineoplastic activity. Vitamin E may also act as an inhibitor of stomach cancer by inhibiting the reactions converting nitrites and nitrates to nitrosourea; possible prevention of gastric cancer by steady consumption of vitamin E and C has been suggested. Vitamin E, an antioxidant with the ability to inhibit free-radical-induced lipid peroxidation, may have some role in human carcinogenesis and cancer treatment, but evidence to support such a role is insufficient. (16 Refs)

### 49. CARCINOGENIC EFFECT OF RADIOACTIVE PRODUCTS.

**Vasilenko Ila**
**No affiliation given**
**Vopr Onkol; 28(1):76-83 1982**

Clinical and experimental data on the carcinogenic effects of the products of nuclear fission (PNF) are reviewed. The incidence and spectrum of PNF-induced tumors depended upon the radiation dosage, the age of the animal, and the nature of PNF. Exposure to chemical carcinogens was shown to enhance the incidence of PNF-induced neoplasms. Administration of thyrostatic agents provided protection against carcinogenic effects of iodine radioisotopes. (32 Refs) (In RUS)

### 50. RECENT DATA ON RADIATION HAZARDS.

**Lindell B**
**Statens stralskyddsinstitut, Stockholm, Sweden**
**Lakartidningen; 79(6):393-397 1982**

The biological effects and hazards of ionizing radiation are discussed. The cancer risk of low radiation doses is subject to great interindividual variations and is affected by many factors, such as the occurrence of other carcinogens and variations in promoting effects. The cancer risk of ionizing radiation is estimated as 0.02 case of death per person, and doses starting with 100 rads. (no Refs) (In SWE)

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# NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

## CHEMICAL CARCINOGENESIS

**1. TOXICITY AND METABOLISM OF ACRYLONITRILE.**
Sapota A, Chmielnicka J
Zaklad Metabolizmu Substancji Toksycznych, Instytut Medycyny Pracy, ul. Teresy 8, 90-950 Lodz, Poland
Med Pr; 32(1):25-33 1981
In POL

**2. A REVIEW OF THE GENOTOXICITY OF FOOD, DRUG AND COSMETIC COLOURS AND OTHER AZO, TRIPHENYLMETHANE AND XANTHENE DYES.**
Combes RD, Haveland-Smith RF
Dept. Biological Sciences, Portsmouth Polytechnic, King Henry I St., Portsmouth, PO1 2DY, Hants, England
Mutat Res; 98(2):171-248 1982

**3. CARCINOGENICITY OF AIRBORNE FINE PARTICULATE BENZO(A)PYRENE: AN APPRAISAL OF THE EVIDENCE AND THE NEED FOR CONTROL.**
Perera F
Natl. Resources Defense Council, Inc., 122 East 42nd St., New York, NY, 10168
Environ Health Perspect; 42:163-185 1981

**4. TOXICOLOGY OF N-NITROSO COMPOUNDS.**
Coulston F, Olajos EJ
Albany Medical Coll., Albany, NY, 12208
Ecotoxicol Environ Saf; 6(1):89-96 1982

**5. CRITICAL REVIEW OF THE MUTAGENIC AND OTHER GENOTOXIC EFFECTS OF DIRECT COAL LIQUEFACTION.**
Kimball RF, Munro NB
Oak Ridge Natl. Lab., Oak Ridge, TN
Critical Review of the Mutagenic and Other Genotoxic Effects of Direct Coal Liquefaction. Available from National Technical Information Service, Springfield, VA, as DE81027859, 216 pp., 1981

**6. CARCINOGENICITY AND ITS EFFECT ON MEDICINAL RESEARCH PROGRAMS IN THE USA.**
Van Ryzin RJ
Pharmaceutical Res. and Development, Sandoz, Inc., East Hanover, NJ, 07936
Med Res Rev; 2(2):153-166 1982

**7. ANTIPROTOZOAL DRUGS (SIDE EFFECTS).**
Nir I
Dept. Pharmacology and Experimental Therapeutics, The Hebrew Univ., Hadassah Medical Sch., Jerusalem, Israel
Side Eff Drugs Annu; (5):278-284 1981

**8. DRUGS USED IN TUBERCULOSIS AND LEPROSY (SIDE EFFECTS).**
Elis J
Inst. Pharmacology, Czechoslovak Acad. Sciences, Albertov 4, Prague 2, Czechoslovakia
Side Eff Drugs Annu; (5):296-297 1981

**9. SEX HORMONES AND RELATED COMPOUNDS, INCLUDING ORAL CONTRACEPTIVES.**
Plotz EJ, Nocke W, Schaefer K, Patt V, Kaulhausen H
Dept. Obstetrics and Gynecology, Univ. Bonn, 5300 Bonn-Venusberg, W. Germany
Side Eff Drug Annu; (5):358-390 1981

## RADIATION CARCINOGENESIS

**10. NEPTUNIUM - THE NEGLECTED ACTINIDE: A REVIEW OF THE BIOLOGICAL AND ENVIRONMENTAL LITERATURE.**
Thompson RC
Biology Dept., Pacific Northwest Lab., Richland, WA, 99352
Radiat Res 90(1):1-32 1982

**11. CARCINOGENIC EFFECT OF RADIOACTIVE PRODUCTS.**
Vasilenko IIa
No affiliation given
Vopr Onkol; 28(1):76-87 1982
In RUS

## DIETARY FACTORS IN CARCINOGENESIS

**12. FIBRES, NUTRITION AND THE GUT.**
Schrijver M, Tytgat GN
Dept. Internal Medicine, Div. Gastroenterology, Univ. Amsterdam, 1e Helmerstraat 104, 1054 EH Amsterdam, The Netherlands
Neth J Med; 25(2):49-55 1982

**13. DIETARY FIBER AND DISEASE.**
Kritchevsky D
Wistar Inst. Anatomy and Biology, Philadelphia, PA
Bull NY Acad Med; 58(3):230-241 1982

**14. ASSESSING HUMAN EPIDEMIOLOGIC DATA ON DIET AS AN ETIOLOGIC FACTOR IN CANCER DEVELOPMENT.**
Enstrom JE
Sch. Public Health, Univ. California, Los Angeles, CA
Bull NY Acad Med; 58(3):313-322 1982

**15. NUTRITION AND CANCER. MECHANISMS OF GENOTOXIC AND EPIGENETIC CARCINOGENS IN NUTRITIONAL CARCINOGENESIS.**
Weisburger JH, Horn C
American Health Foundation, Valhalla, NY, 10595
Bull NY Acad Med, 58(3):296-312 1982

## EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

**16. THE AH LOCUS, A MULTIGENE FAMILY NECESSARY FOR SURVIVAL IN A CHEMICALLY ADVERSE ENVIRONMENT: COMPARISON WITH THE IMMUNE SYSTEM.**
Nebert DW
Developmental Pharmacology Branch, National Inst. Child Health, NIH, Bethesda, MD, 20205
Adv Genet; 21:1-52 1982

## ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN CARCINOGENESIS

**17. SKIN CANCER: OCCUPATIONAL CAUSES.**
Bickers DR
Dept. Dermatology, Case Western Reserve Univ., Cleveland, OH
Consultant; 22(4):392-393,397,400-401 1982

**18. OCCUPATIONAL AND ENVIRONMENTAL HEALTH PROBLEMS OF THE DEVELOPING OIL SHALE INDUSTRY: A REVIEW.**
Rom WN, Lee JS, Craft BF
Rocky Mountain Center Occupational and Environmental Health, Dept. Internal Medicine, Family and Community Medicine, Univ. Utah Sch. Medicine, Bldg. 512 Salt Lake City, UT 84112
Am J Indust Med; 2(3):247-260 1981

**19. POLYCYCLIC AROMATIC HYDROCARBONS IN THE OCCUPATIONAL ENVIRONMENT: WITH SPECIAL REFERENCE TO BENZO[A]PYRENE MEASUREMENTS IN SWEDISH INDUSTRY.**
Lindstedt G, Sollenberg J
Chemistry Dept., Natl. Board Occupational Safety and Health, S-171 84 Solna, Sweden
Scand J Work Environ Health; 8(1):1-19 1982

**20. GENETIC RISKS AND ENVIRONMENTAL SURVEILLANCE: EPIDEMIOLOGICAL ASPECTS OF MONITORING INDUSTRIAL POPULATIONS FOR ENVIRONMENTAL MUTAGENS.**
Buffler PA, Aase JM
Sch. Public Health, Univ. Texas Health Science Center at Houston, P.O. Box 20186, Houston, TX, 77025
JOM; 24(4):305-314 1982

**21. OSHA AT THE THRESHOLD: SETTING PERMISSIBLE EXPOSURE LEVELS FOR KNOWN CARCINOGENS AFTER AMERICAN PETROLEUM INSTITUTE.**
Blackmar GB
No affiliation given
San Diego Law Rev; 18(4/5):633-661 1981

**22. CARCINOGENESIS: PROBLEMS AND PARADOXES. THE 1981 GEORGE H. GEHRMANN LECTURE.**
Kotin P
4505 South Yosemite, 339, Denver, CO, 80237
JOM; 24(4):290-294 1982

## CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

**23. MODIFICATIONS OF CHROMATIN STRUCTURE IN CONTROL OF GENE EXPRESSION.**
Hull LA
104 Depot St., New Sharon, IA, 50207
Med Hypotheses; 8(2):113-133 1982

**24. PLASMINOGEN ACTIVATORS IN NEOPLASTIC CELLS.**
Goloborod'ko OP, Veremeenko KN
A. I. Kolomiichenko Res. Inst. Otolaryngology, Kiev USSR
Eksp Onkol; 4(1):3-7 1982
In RUS

**25. TUMOR PROMOTION BY REGENERATIVE EPIDERMAL HYPERPLASIA IN MOUSE SKIN.**
Argyris TS
Dept. Pathology, Upstate Medical Center, State Univ. New York, Syracuse, NY, 13210
J Cutan Pathol; 9(1):1-18 1982

**26. SEX HORMONES AND LIVER CANCER.**
Williams GM
Naylor Dana Inst. for Disease Prevention, New York Medical Coll., Valhalla, NY
Lab Invest; 46(3):352-356 1982

## METHODOLOGY IN CARCINOGENESIS RESEARCH

**27. UTILIZATION OF CELL TRANSFORMATION TESTS IN THE DETECTION OF CHEMICAL CARCINOGENS.**
Elias Z, Cavelier C
Institut National de Recherche, Centre de Recherche de Nancy, avenue de Bourgogne, F-54500 Vandoeuvre-les-Nancy, France
Bull Cancer (Paris); 69(1):33-57 1982
In FRE

**28. FAILURES AND CRITIQUE OF THE BEIR III LUNG CANCER RISK ESTIMATES.**
Cohen BL
Univ. Pittsburgh, Pittsburgh, PA, 15260
Health Phys; 43(3):267-284 1982

## OTHER REVIEWS IN CARCINOGENESIS

**29. CANCER. AN INTRODUCTION.**
Creasey WA
Dept. Pharmacology, Univ. Pennsylvania Sch. Medicine, Philadelphia, PA
Cancer. An Introduction. New York, Oxford University Press, 271 pp., 1981

**30. CANCER 1980: ACHIEVEMENTS, CHALLENGES, AND PROSPECTS.**
Clark RL
Univ. Texas System Cancer Center, M.D. Anderson Hosp. and Tumor Inst., 6723 Bertner Ave., Houston, TX, 77030
Cancer; 49(9):1739-1745 1982

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# ICRDB CANCERGRAM

# RADIATION CARCINOGENESIS

SERIES CK06 No. 82/10
OCTOBER, 1982

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## RADIATION CARCINOGENESIS IN HUMANS

### 1. STUDIES OF THE MORTALITY OF A BOMB SURVIVORS. 7. MORTALITY, 1950-1978: PART I. CANCER MORTALITY.

**Kato H, Schull WJ**
**Radiation Effects Res. Foundation, Hiroshima, Japan**
**Radiat Res; 90(2):395-432 1982**

Mortality of survivors of the atomic bombing of the cities of Hiroshima and Nagasaki during World War II is updated to include the years 1975-1978. The excess in leukemia deaths continued to decrease during these yr from the peak in 1950-1954, and in 1975-1978 an increased mortality with dose was observed only in Hiroshima. Cancers other than leukemia have increased yearly from about 1960 and, averaged over all periods, the risk of these cancers now equals (Nagasaki) or exceeds (Hiroshima) that of leukemia. The risks of lung, breast, and stomach cancers, which were shown be significantly increased in the yr 1950-1974, have continued to rise in 1975-1978, but there has been no apparent additional increase in risk in 1975-1978 for esophageal or urinary tract cancers, which had increased previously. An elevated risk of colon cancer has

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become newly evident. The significant increase with dose observed for malignant lymphoma in the previous report appeared in retrospect to be spurious, stemming possibly from the inclusion of multiple myeloma. No increased risk of uterine cancer has been seen. A greater excess of a variety of tumors was observed in Hiroshima than in Nagasaki in all periods combined. The significance of the relationship between radiation and cancer is discussed. (17 Refs)

### 2. SECOND MALIGNANT NEOPLASMS IN PATIENTS SUCCESSFULLY TREATED FOR HODGKIN'S DISEASE: A CANCER AND LEUKEMIA GROUP B STUDY.

**Glickman AS, Pajak TF, Gottlieb A, Nissen N, Stutzman L, Cooper MR**
**Dept. Radiation Oncology, Rhode Island Hosp., Providence, RI, 02902**
**Cancer Treat Rep; 66(4):1035-1044 1982**

The recent analyses by the Cancer and Leukemia Group B (CALGB) of patients with advanced Hodgkin's disease entered in CALGB treatment protocols between 1966 and 1974 have substantiated the recognized high susceptibility of these patients to second malignant neoplasm. Protocols 6604, 6712, 6951, and 7251 included radiation therapy and/or chemotherapy with alkylating agents such as mechlorethamine and chlorambucil or nitrosoureas, vinca alkaloids, and procarbazine as induction agents, plus or minus maintenance therapy with vinblastine, or chlorambucil or a repetition of the induction program. The risk of a second malignant neoplasm attributable to each component of curative treatment was analyzed: 798 of 1332 evaluable patients achieved complete remission, with a mean followup of 46 mo. For 27 of these 798 patients, development of a second malignant neoplasm terminated the complete response. Ten patients developed acute myeloid leukemia (AML). For AML, induction chemotherapy with a mechlorethamine-containing regimen, followed by chlorambucil maintenance therapy, had the highest relative risk ratio and life-table estimate. Mechlorethamine without chlorambucil maintenance was not a significant hazard, but chlorambucil without mechlorethamine was associated with a relative risk ratio of 234 and a life-table estimate of 9%. Radiotherapy was not a significant hazard when added to the chemotherapy regimens. For the non-AML second malignant neoplasms, none of the chemotherapy regimens was a greater risk than the others, with a relative risk of 2.8. The addition of radiotherapy significantly increased the incidence of such neoplasms. Patients of all ages had a significant risk of AML but not of the other second malignant neoplasms; however, because of the increasing rate of second malignant neoplasms with the intervening years, the full extent of the risk may not be appreciated for another decade. (13 Refs)

### 3. USE OF THE CANADIAN MORTALITY DATA BASE FOR EPIDEMIOLOGICAL FOLLOW-UP.

**Smith ME, Newcombe HB**
**Occupational and Environmental Health Unit, Vital Statistics and Disease Registries Section, Statistics Canada, 17th Floor, R.H. Coats Building, Tunney's Pasture, Ottawa, Ontario, K1A OZ5, Canada**
**Can J Public Health; 73(1):39-46 1982**

The Canadian Mortality Data Base (CMDB) contains all Canadian death registrations dating from 1950. The CMDB contains personal identifying information, is machine-readable and in microfiche and microfilm form, and is sequenced and consolidated to facilitate manual searching. Several follow-up studies have been performed for various 'at-risk' groups, including infant death-birth linkages, isoniazid and cancer in tuberculosis patients, a 10% sample of the Canadian labor force, and fluoroscopy and cancer in tuberculosis patients. Searches presently in progress involve nickel workers, uranium workers, Ontario workers, particularly miners, Nutrition Canada Survey participants, Ontario morticians, who have high levels of exposure to formaldehyde, railway workers, childbearing women and breast cancer, Alberta cancer files, and fluospar mining in Newfoundland. Several other searches involving the data base are under negotation, including radiation-exposed workers. The CMDB has the potential for other searches involving individual linear follow-up to investigate health problems associated with diet, food additives, pharmaceuticals, water supply, and workplace conditions. The system is economical and need not threaten personal privacy. (46 Refs)

### 4. EPIDEMIOLOGY OF THYROID CANCER.

**Riccabona G**
**Universitatsklinik fur Nuklearmedizin, Innsbruck, Austria**
**Praxis; 71(13):523-525 1982**

The incidence of thyroid cancer (TC) is not related to the incidence of goiter. In TC-endemic areas aggressive, undifferentiated forms of TC predominate. Prophylactic therapy with iodized salt increases the proportion of less malignant forms. 'Cold' nodules have a malignancy rate of 6% in endemic areas, compared with 30% in nonendemic areas. Males and older persons have an increased risk of TC. Pathogenic factors include slightly increased thyroid stimulating hormone levels and childhood irradiation. (9 Refs) (In GER)

### 5. BREAST IRRADIATION AND FUTURE RISK, EG CARCINOGENESIS (MEETING ABSTRACT)

**Levitt SH**
**Department of Therapeutic Radiology, University of Minnesota Hospitals, Minneapolis, MN**
**Seventeenth Annual San Francisco Cancer Symposium, February 27-28, San Francisco, California West Coast Cancer Foundation; 1982**

A major concern for physicians treating breast cancer patients with conservative surgery and radiation therapy is the possibility of the development of an increased incidence of second cancer in the contralateral breast and the treated breast. An analysis of the epidemiologic data related to the development of breast cancer was carried out, and the relative risks related to the dose of irradiation, the type of irradiation, the intent of the irradiation, and the age of the patient will be discussed. In addition, the clinical studies with the largest number of patients treated with radiation following breast cancer surgery with minimal and radical intent were reviewed. Based on these studies, the extent of risk of developing a second primary in the homolateral or contralateral breast is found to be minimal and not of such consequence that it would contraindicate the use of conservative surgery and radiation in the treatment of breast cancer. (no Refs)

### 6. HEAD AND NECK MALIGNANCY IN A YOUTHFUL POPULATION (MEETING ABSTRACT)

**Clark RM, Rosen IB**
**University of Toronto, Toronto, Ontario, Canada**
**Joint Meeting of the Society of Surgical Oncology and Society of Head and Neck Surgeons, April 18-23, 1982, Marco Island, Florida. The Society of Surgical Oncology and the Society of Head and Neck Surgeons 265 pp., 1982.**

Since malignancy in the head and neck area usually afflicts those of middle age and older, little knowledge and experience has been established in this disease affecting the younger population. A retrospective survey of 351 patients under 35 with head and neck cancer was carried out and in which 118 cases occurred under the age of 25. Sites studied included lip 49, tongue 21, salivary 14, oral cavity 24, nasopharynx 89, oropharynx 9, laryngopharynx 4, nose 7, ear 13, sinus 25, larynx 36. The median age range varied from 6-32 years of age. Mucosal cancer was usually treated by primary irradiation and salvage surgery and salivary disease was treated by primary surgery and adjuvant irradiation therapy. Survival rates on a five year basis include lip, 93%, tongue, 56%, salivary 91%, nasopharynx 55%, oropharynx 86%, laryngopharynx 1/2 % , sinus 45%, larynx 93% Examination of etiology did not reveal any consistent presence of exposure to radiation, tobacco, alcohol addiction or genetic predisposition. It would appear that head and neck malignancy in the young is a substantial entity in head and neck surgical practice requiring wider acquaintance with this group and site individualization of treatment. The favorable five year results support the concept of aggressive treatment particularly since this group of patients is capable of tolerating adjuvant therapy where indicated. (no Refs)

### 7. EPIDEMIOLOGIC SURVEY OF BLADDER CANCER IN GREATER NEW ORLEANS (MEETING ABSTRACT)

**Sullivan JW**
**No affiliation given**
**77th Annual Meeting of the American Urological Association, Inc. May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.**

The primary ancestry of the cases and the controls was not statistically different, but the Jewish population had a significantly greater increased incidence of bladder cancer. Overall, a significantly greater number of cases smoked filtered cigarettes, commenced consumption of artifical sweetened beverages at an ealier age, drank artificial sweetened beverages for a greater number of years, consumed a greater number of glasses of artificial sweetened beverages per week and related a history of urinary tract infections. A significantly increased incidence of bladder cancer was noted in individuals employed by certain types of companies, by certain job titles, and by certain job material handled. Analysis of the data failed to show any significant difference in years of consumption of coffee, amount of various types of coffee or tea consumed, consumption of various alcoholic and non-alcoholic beverages including source of drinking water, usage of hair dye, incidence of diabetes mellitus, family history of urinary cancer, history of pelvic irradiation or bladder stones. (no Refs)

## EXPERIMENTAL RADIATION CARCINOGENESIS

### 8. SUPPRESSOR T LYMPHOCYTES CONTROL THE DEVELOPMENT OF PRIMARY SKIN CANCERS IN ULTRAVIOLET-IRRADIATED MICE.

**Fisher MS, Kripke ML**
**Cancer Biology Program, NCI, Frederick Cancer Res. Facility, Frederick, MD, 21701**
**Science; 216(4550):1133-1134 1982**

Exposure of mice to ultraviolet radiation results in the development of suppressor T lymphocytes in lymphoid organs, followed by the appearance of primary skin cancers. The presence or absence of these suppressor lymphocytes determines whether or not primary cancers will develop in the ultraviolet-irradiated skin. This demonstrates the importance of immunological regulatory pathways in carcinogenesis and provides an example of immunological surveillance. (Author abstract) (18 Refs)

### 9. WHOLE-THORAX RADIATION LETHALITY IN PENICILLAMINE-TREATED MICE.

**Ward WF, Shih-Hoellwarth A, Pearlman HG, Kepka AG**
**Dept. Radiology, Northwestern Univ. Medical Sch., Chicago, IL, 60611**
**Radiat Res; 90(2):321-329 1982**

Male Sch(ICR)BR mice were observed for 1 yr after whole-thorax irradiation (10-20 Gy 60 cobalt gamma rays to a 1.5 cm whole-thorax port) in order to assess the effect of penicillamine (PEN) on both early and late lung injury. Half of the 451 mice studied were fed standard powdered feed and half received feed containing PEN at 2 mg/kg/day. Twenty-three (10 control diet and 13 PEN-treated) mice developed histologically confirmed malignant tumors at necropsy and were eliminated from the study. Mortality increased linearly with increasing radiation dose in both control and PEN-treated mice. Mean survival time was inversely proportional to radiation dose but was not influenced by PEN-treatment. In sham-irradiated mice, PEN suppressed body wt gain throughout the 1-yr observation period. In irradiated animals, body wt was inversely proportional to radiation dose in both control and PEN-treated animals. PEN did increase body wt for the first 6 mo post-irradiation, however. Drug treated mice thus appeared to have better endured the acute phase of the radiation reaction. (28 Refs)

### 10. PREVENTION OF THE BENZO(ALPHA)PYRENE PHOTOCARCINOGENIC EFFECT BY B-CAROTENE AND CANTHAXANTHINE (MEETING ABSTRACT)

**Santamaria L, Bianchi A, Arnaboldi A, Andreoni L**
**University of Pavia, Pavia, Italy**
**Med Biol Environ; 9(1):113 1981**

Beta-carotene (C) and canthaxanthine (CX) were perorally administered to female Swiss albino mice, with daily diet. One month after initiating the above dietary treatment, the mice were given additional administrations of C and CX by catheter twice a week. They were then painted with benzopyrene (BP) and were either exposed to long UV light (300-400 nm with maximum output at 365 nm) twice a week or kept in the dark. Tumors appeared earlier and grew more rapidly in BP-painted and long UV irradiated mice; thus, confirming the 'BP photocarcinogenic effect'. C and CX substantially prevented such an effect (respectively, 79% and 66%, as compared to carcinogenesis in the dark), demonstrating the relevance of carotenoids in the development of rational programs of skin cancer prevention in occupational medicine. (no Refs)

### 11. POSSIBLE ROLE OF NK CELLS IN RADIATION LEUKEMOGENESIS (MEETING ABSTRACT)

**Datta SK, Priest EL, Trentin JJ**
**Baylor College of Medicine, Houston, TX, 77030**
**Fed Proc; 41(3):316 1982**

Kaplan et al demonstrated that fractionated sublethal whole body irradiation of C57BL/6 mice, resulted in development of thymic-lymphoma-leukemia, but a post-irradiation transfusion of bone marrow prevented it. To investigate a possible role of natural killer (NK) cells in radiation leukemogenesis, we studied the effect of fractionated irradiation of C57BL/6 mice on NK cell activity and development of thymic lymphoma. Groups of 4-6 week old C57BL/6 mice were exposed to 225 rads of whole body irradiation, once a week for 4 weeks. Following the last radiation exposure, one group of mice was transfused with 10(7) C57 bone marrow cells. Marrow-transfused, non-transfused and control mice were tested at weekly intervals, for spleen NK cell-lysis of YAC-1 lymphoma target cells, with or without 1 or 5 days prior intraperitoneal injection of Poly I:C or Corynebacterium parvum (CP), respectively. NK cell activity was depressed from 1 to 8 weeks post treatment in fractionally-irradiated mice but was quickly restored to control levels in bone marrow transfused mice. Both CP and Poly I:C treatment partially restored NK cell activity of mice exposed to leukemogenic irradiation. The development of thymic lymphoma is being followed. The results suggest that NK cells may play a role in the control of radiation leukemogenesis. Similar results have recently been published by Parkinson et al. (no Refs)

### 12. CYTOTOXICITY AND SUPPRESSION DURING RADIATION AND RADLV-INDUCED LEUKEMOGENESIS (MEETING ABSTRACT)

**Yefenof E, Kedar E**
**The Lautenberg Center for General and Tumor Immunology, Hebrew, University-Hadassah Medical School Jerusalem 91 010, Israel**
**Fed Proc; 41(3):417 1982**

Adult C57BL/6 mice exposed to fractionated x-irradiation or inoculated with the highly leukemogenic variant of the Radiation Leukemia Virus (A-RadLV) develop high incidence lymphatic leukemias within 3-6 months. A-RadLV-induced, but not x-ray-induced lymphomas, can elicit cytotoxic responses in vitro in lymphocytes of preimmunized syngeneic mice, a reaction that is dependent on the expression of membrane associated viral antigenicity. As soon as 5 days after A-RadLV inoculation and during the entire leukemogenic process suppressor T cells are detectable in the spleen that are capable of specifically abrogating generation of syngeneic anti-tumor cytotoxic cells in vitro. These suppressor cells are generated directly by the virus, independently of initiation of the leukemogenic process. Mice exposed to fractionated x-ray irradiation or inoculated with the low leukemogenic D-RadLV variant do not develop suppressor cells and their splenocytes can be stimulated in vitro to generate cytotoxicity towards RadLV-induced leukemias. These findings suggest that: (a) although RadLV has been isolated from radiation induced leukemias, x-ray and RadLV-induced leukemogenesis do not seem to involve a common viral etiology; (b) induction of tumor specific suppression by A-RadLV may be essential for tumor progression; and (c) the low leukemogenic potential of D-RadLV may be attributed to its inability to trigger host's suppressor cells. (no Refs)

### 13. TUMOR DEVELOPMENT IN X-IRRADIATED TRANSPLANTS OF NORMAL AND HYPERPLASTIC MOUSE MAMMARY GLANDS (MEETING ABSTRACT)

**Faulkin LJ, Mitchell DJ, Cardiff RD, Goldman M**
**Department of Anatomy, School of Veterinary Medicine, University of California, Davis, CA, 95616**
**Proc Am Assoc Cancer Res; 23:921 1982**

The risk of increasing tumor development following exposure of the mammary gland to x-rays is being investigated using the inbred BALB/c mouse and several serially passaged lines of hyperplastic mammary tissue. To avoid the complications of whole body exposure, the mammary tissue was transplanted to non-irradiated hosts. The donor tissue was exposed to whole body x-irradiation of 0, 25, 75, 225 and 675 RAD. Within an hour 0.5mm cubes of tissue were excised and transplanted to host gland free inguinal fat pads. The 60 to 100 transplants in each dose group were observed weekly for tumor development. Transplants of mammary ducts have been in the host mice for over one year and no tumors have been observed in any of the dose groups. The hyperplastic outgrowth line Z5C1, has shown a response in the cummulative tumor incidence curves that is proportional to dose. The slope of the incidence curves for 0, 25, and 75 RAD are not different. However, the latency period is decreased 4 and 5 weeks for the 25 and 75 RAD groups, respectively. In the 225 and 675 dose groups the latency period is increased, however, the slope of the incidence line is much steeper and reaches the 50% incidence level before the lower doses or controls. Studies with other hyperplastic outgrowth lines are in progress and preliminary data suggests a variable response for each outgrowth line depending on its normal tumor incidence rate. (no Refs)

## EFFECTS OF IRRADIATION ON CHROMOSOMES AND DNA

### 14. CHROMOSOMAL RADIATION SENSITIVITY IN ATAXIA TELANGIECTASIA LONG-TERM LYMPHOBLASTOID CELL LINES.

**Littlefield LG, Colyer SP, Joiner EE, DuFrain RJ, Frome E, Cohen MM**

**Cytogenetics Lab., Medical and Health Sciences Div., Oak Ridge Associated Univ., P.O. Box 117, Oak Ridge, TN, 37830**

**Cytogenet Cell Genet; 31(4):203-213 1981**

Elevated frequencies of spontaneous chromosome breakage and hypersensitivity to radiation induced chromosome damage are characteristic findings in cultured lymphocytes and skin fibroblasts of patients with ataxia telangiectasia (AT). To determine whether long-term AT lymphoblastoid cells (B-lymphocytes) which do not express spontaneous chromosomal instability, exhibit increased chromosomal radiation sensitivity, four AT lymphoblastoid cell lines were exposed to various doses of 250 kVp x-rays during G2. At doses of 25 and 50 rad, the AT cells exhibited a 2-3 fold increase in radiation damage relative to that observed in B-cell lines or PHA stimulated lymphocytes from normal donors, while at 100 rad, the AT cells demonstrated approx 1.5x more lesions. These findings suggest that the genetic (or other) factors responsible for increased chromosomal radiation sensitivity in AT lymphocytes and fibroblasts also operate in long-term lymphoblastoid AT cells. (Author abstract) (36 Refs)

### 15. CYTOGENETIC ANALYSIS OF PERIPHERAL BLOOD LYMPHOCYTES IN MEN SUBJECTED TO EXPOSURE TO SMALL DOSES OF IONIZING RADIATION.

**Petrova SP**
**No affiliation given**
**Med Radiol (Mosk); 27(3):70-73 1982**

To evaluate the biological effects of small doses of ionizing radiation, the peripheral blood lymphocytes from 30 men (29-44 yr old) who had a 4-17-yr exposure to gamma radiation were subjected to cytogenetic analysis. The annual radiation exposure was 0.5-20.0 mSv (no further details). The frequency of chromosome aberrations in exposed group did not differ from that in controls (0.67% and 0.35%, respectively). (15 Refs) (In RUS)

### 16. STRUCTURAL CHANGES IN MAMMALIAN CELL DNA INDUCED BY LOW-DOSE X-RAY DAMAGE AND SUBSEQUENT POSTIRRADIATION INCUBATION IN THE PRESENCE AND ABSENCE OF CAFFEINE.

**Wun KL, Shafer RH**
**Dept. Pharmaceutical Chemistry, Sch. Pharmacy, Univ. California, San Francisco, CA, 94143**
**Radiat Res; 90(2):310-320 1982**

Experiments on low-dose (30-2,000 rad) x-ray-induced damage in rat 9L cells in vitro and subsequent posttreatment irradiation measured under neutral (pH 7) conditions are described. Results indicated that the principal retardation time of DNA in neutral lysates was sensitive to x-irradiation of the cells. The retardation time increased by about a factor of seven in the dose range of 0-1,000 rad, the major portion of the increase occurring with the first 300 rad. The biphasic nature of the response to increasing doses of radiation appeared to be unique to the viscoelastic method utilized. The viscoelastic retardation time showed a complicated pattern reflecting different structures of DNA during postirradiation incubation. No indication of loss of large DNA during postirradiation incubation was observed. Results were interpreted as suggesting conformational changes in damaged DNA during repair. Post-irradiation incubation in the presence of 0.5 milliM caffeine resulted in inhibition of DNA repair. (29 Refs)

### 17. KINETICS OF REPAIR OF DNA SINGLE-STRAND BREAKS IN CULTURED MAMMALIAN CELLS. PART I. THE DEPENDENCE ON IRRADIATION DOSE AND CELL CYCLE STAGE.

**Vexler FB, Kublik LN, Eidus LK, Vexler AM**
**Inst. Biological Physics, U.S.S.R. Acad. Sciences, Pushchino, Moscow Region, 142292, USSR**
**Int J Radiat Biol; 41(4):453-457 1982**

Kinetics of repair of DNA single-strand breaks were examined in asynchronous cultures of Chinese hamster cells and in cells synchronized at the G1 stage after irradiation with doses of 15 and 200 grays (Gy), which induce reproductive and interphase death of cells, respectively. Irradiation led to practically the same DNA degradation independent of cell cycle stage. In all experiments with asynchronous cultures, repair started immediately after irradiation with 15 and 200 Gy and did not depend on the pH of the medium in the range 6.5-8.0. The major part of the strand breaks repaired quickly enough. Following exposure to 15 Gy, the repair proceeded at a constant rate in both cultures; however, the repair rate was twice as low in synchronous as in asynchronous cultures. After irradiation with 200 Gy, the repair processes in both cultures started with the rates close to those at a lower dose. However, 5 min later, the repair rates became about 5-6x lower in asynchronous cultures; in asynchronous cultures, it was 2x as low as that in asynchronous cultures. Then the rates remained practically constant in both cultures. (14 Refs)

### 18. EFFECT OF PULSE-PERIODIC LASER UV IRRADIATION OF LOW INTENSITY ON PROLIFERATING AND RESTING TUMOR CELLS.

**Karu TI, Kalendo GS, Letokhov VS, Lobko VV**
**Res. Center Technological Lasers, Moscow, USSR**
**Dokl Akad Nauk SSSR; 262(6):1498-1501 1982**

Irradiation of HeLa cells in the logarithmic growth phase (proliferating cells) or in the stationary phase (resting cells) with low intensity pulse UV laser produced decrease of DNA synthesis permeability of cell membrane in proliferating cells. In the resting cells, pulse laser irradiation stimulated DNA synthesis and increased permeability of cell membranes for 3H-thymidine. Irradiation with continuous lasers inhibited DNA synthesis in proliferating cells but did not affect DNA synthesis in resting cells. (4 Refs) (In RUS)

## OTHER CELLULAR EFFECTS OF IRRADIATION

### 19. INHIBITORY EFFECTS OF VARIOUS OXYGENATED STEROLS ON THE DIFFERENTIATION AND FUNCTION OF TUMOR-SPECIFIC CYTOTOXIC T LYMPHOCYTES.

**Spangrude GJ, Sherris D, Daynes RA**
**(c/o Daynes) Dept. Pathology, Univ. Utah Medical Center, Salt Lake City, Utah, 84132**
**Transplantation; 33(5):482-491 1982**

These studies were undertaken to determine the effect of various oxygenated sterols (representing a number of known cholesterol-derived photoproducts) on the generation (afferent) and function (efferent) of cytotoxic T lymphocytes (CTLs). Cell-mediated immune responses which result in the generation of both alloantigen-specific and syngeneic tumor-specific CTLs were evaluated. The results of our studies established the following points: (1) the afferent phase of an immune response is particularly sensitive to the effects of some cholesterol photoproducts while other oxidized sterol derivatives, known to exist in skin following UV light (UVL) exposure, have minimal influence on the generation of CTL responses; (2) the only known carcinogenic photoproduct of cholesterol (cholesterol alpha-oxide) is a very weak inhibitor of lymphocyte function and (3) presentation of oxygenated sterols via liposome membranes is 10-fold more effective than their administration in soluble form; (4) 25-hydroxycholesterol and 20alpha-hydroxycholesterol were found to be the most potent inhibitors, causing a parallel depression in lymphocyte proliferation, CTL activity, and endogenous sterol biosynthesis, and (5) 7beta- and 7alpha-hydroxycholesterol functioned in a unique manner, causing an abrogation of CTL activity without depressing proliferative responses and endogenous sterol biosynthesis to a significant degree. These studies represent the first time that an attempt has been made to evaluate a possible biochemical basis for immune suppression known to precede experimental UVL carcinogenesis. Our results suggest that some, but not all, of the oxidation products of cholesterol found in skin following UVL irradiation exert an influence on immune responses. Derivatives of cholesterol could be partially responsible for the alterations in immunological potential of the UVL-exposed host. The induced presence of an inhibitor of CTL differentiation or function at a time following UVL tumor emergence may play a role in this process by providing an early tumor escape mechanism. (37 Refs)

## 20. EVIDENCE FOR TWO FUNCTIONALLY DISTINCT CROSS-REACTIVE TUMOR ANTIGENS ASSOCIATED WITH ULTRAVIOLET LIGHT AND CHEMICALLY INDUCED TUMORS.

**Roberts LK, Lynch DH, Daynes RA**
**(c/o Daynes) Dept. Pathology, Univ. Utah Medical Center, Salt Lake City, UT. 84132**
**Transplantation; 33(4):352-360 1982**

Experiments were conducted to determine the distribution and function of common tumor antigens shared by UV light-, benz[a]pyrene (BP)-, and methylcholanthrene (MCA)-induced tumors. When lymph node cells were removed from UV, BP, or MCA tumor-immune mice and held in tissue culture for 4 days, a population of cytotoxic T lymphocytes (CTLs) emerged that were capable of lysing a battery of different tumor targets. These CTLs displayed crossreactive in vivo activity in Winn-type assays. These CTLs recognized tumor-associated antigens (TAAs) common to both UV and chemically induced tumors. These common TAAs were incapable of eliciting cross-protective tumor immunity when tumor immunizations and challenges were made entirely in vivo. The state of cross-protective immunity within hyperimmune mice is directed toward shared tumor-associated transplantation antigens (TA-TAs). These particular determinants are related to the induction etiology of the tumor. Previous reports have suggested that the suppressor T lymphocytes (Ts cells) present in UV-treated animals possess functional specificity for the common TATAs expressed by UV tumors. We believe that UV-induced Ts cells recognize the common TAAs shared by UV and MCA tumors. Collectively, these data define at least two different classes of common tumor antigens expressed by UV and chemically induced tumors. These antigenic determinants are functionally defined as the TATAs and the common TAAs. The shared TATA function in vivo as rejection antigens and are restricted to tumors induced by the same carcinogenic agent. In contrast, the common TAAs shared by UV and chemically induced tumors are not only recognized by CTLs but more importantly function as immunoregulatory determinants. The importance of these common tumor antigens in host-tumor interactions is discussed. (32 Refs)

## 21. SURVIVAL CURVES OF IRRADIATED GLUTATHIONE-DEFICIENT HUMAN FIBROBLASTS: INDICATION OF A REDUCED ENHANCEMENT OF RADIOSENSITIVITY BY OXYGEN AND MISONIDAZOLE.

**Midander J, Deschavanne PJ, Malaise EP, Revesz L**
**Dept. Tumor Biology II, Karolinska Inst., 104 01 Stockholm, Sweden**
**Int J Radiat Oncol Biol Phys; 8(3/4):443-446 1982**

The role of glutathione (GSH) in the response of hypoxic cells to misonidazole (MA) was studied in nontransformed GSH-producing (GSH+) and GSH-deficient (GSH-) fibroblasts. GSH- fibroblasts were derived from a patient with 5-oxoprolinuria; GSH+ fibroblasts were derived from the patient's healthy brother. The mean GSH level was 11.55 +-1.10 nanomoles/mg protein (nmol/mg) for GSH+ cells and 0.72 +-0.17 nmol/mg for GSH- cells. The mean level of total nonprotein sulfhydryl compounds was 12.87 +-1.37 nmol/mg for GSH+ cells and 5.98 +-1.23 nmol/mg for GSH- cells. For hypoxic irradiations cell cultures were flushed for 15 min, including irradiation time, with humidified argon. Cultures treated with MA were exposed to 8 milliM MA for 2 hr. For oxic irradiation cultures were exposed to air or 100% O2 for 24 prior to irradiation. Irradiation used 137Cs gamma-rays at a dose rate of 0.8 Gray/min. Survival curves of GSH- cells in air and in O2 were similar, with dose modifying factors (DMF) of 1.06 and 1.07 at survival levels of 10(-1) (S1) and 10(-2) (S2), respectively. Survival of GSH+ cells was less in O2 than in air, with DMF of 1.25 at S1 and 1.21 at S2. Survival curves for GSH+ and GSH- cells were similar in O2. Radiosensitivity of both strains under hypoxic conditions was increased by MA, but the increase was much greater for GSH+ cells than for GSH- cells. Data are consistent with the competition theory, by which oxygen, which fixes radiation damage, and GSH, which repairs radiation damage, compete for radicals produced by irradiation. GSH evidently is an important factor in the response of hypoxic cells to irradiation in the presence or absence of MA. (10 Refs)

## 22. FURTHER STUDIES ON THE SURVIVAL OF NON-PROLIFERATING HUMAN DIPLOID FIBROBLASTS IRRADIATED WITH ULTRAVIOLET LIGHT.

**Chan GL, Little JB**
**Dept. Pathology, Harvard Medical Sch. and Sidney Farber Cancer Inst., 44 Binney St., Boston, MA, 02115**
**Int J Radiat Biol; 41(4):359-368 1982**

Labelling index data showed that in AG1518 cells, a diploid human fibroblast strain, there was a lag period of at least 14 hours between subculture from the density-inhibited plateau phase of growth and entry into DNA synthesis. Cells irradiated with 254 nm wavelength UV light 8 hr after subculture did not exhibit the same degree of resistance as cells irradiated in plateau phase and subcultured immediately. When cells were arrested from proliferation by maintenance in an arginine and glutamine deficient medium for 72 hr, they were nearly as resistant to UV light as plateau phase cells although maintenance in this medium for 24 hr after irradiation supported further recovery only after low UV doses. One strain of Cockayne syndrome fibroblasts was found to be resistant to UV light in plateau phase while another strain was found to have the same survival response whether it was irradiated in the plateau or log phase of growth. (Author abstract) (16 Refs)

## 23. DIVISION PROBABILITY AND DIVISION DELAY IN DIPLOID SYRIAN HAMSTER CELLS FOLLOWING A RANGE OF X-RAY DOSES.

**Joshi GP, Nelson WJ, Revell SH, Shaw CA**
**Physics Dept., Inst. Cancer Res., Sutton, Surrey, England**
**Int J Radiat Biol; 41(4):443-448 1982**

Estimates of the likelihood that cultured diploid Syrian hamster line BHK-21 C13 cells reach post-irradiation mitosis after single x-ray doses in the range of 0.2-3.8 grays (Gy) are presented along with measurements of the mean duration of irradiated interphase observed in the same cell samples. The progressions of 200 cells were individually followed at each of eight x-ray dose levels and compared with an unirradiated 200-cell sample. The probability of reaching mitosis M1 remained close to unity over the whole x-ray dose range: the highest fraction of non-dividers observed was 4/200 at 3.0 Gy. The mean interphase duration, derived from all cells (except non-dividers), had a slope of 1.32 hr/Gy with a zero-dose value of 10.17 hr. The increases in dose-proportionate delay were only detectable in each cell sample as a whole. The individual cells of all irradiated samples were indistinguishable from those of the control sample and gave no sign of abnormal behavior. Cells within irradiated samples varied widely in their delay response. (15 Refs)

### 24. DOSE CURVES FOR RADIATION INJURY OF HEMATOPOIETIC SYSTEM AFTER LONG-TERM RADIATION EXPOSURE.

**Gorlov VG, Neman OV**
**No affiliation given**
**Kosm Biol Aviakosm Med; 16(1):86-89 1982**

The effects of long-term radiation exposure on the hematopoietic system were studied in random-bred rats. The animals were subjected to continuous irradiation at 300, 100, and 50 R/day. The state of the hematopoiesis was evaluated after accumulation of a total dose of 30-2,700 R. The decrease of the cellularity of bone marrow depended upon the total dose and dose rate. The most radiosensitive hematopoietic cells were peripheral blood lymphocytes, reticulocytes, and blood platelets (15 Refs) (In RUS)

## THEORETICAL ASPECTS OF RADIATION CARCINOGENESIS

### 25. MOLECULAR EVENTS BASIC TO CELLULAR RADIATION RESPONSE.

**Kolodny GM**
**Radiology Res. Lab., Massachusetts General Hosp., Boston, MA**
**Molecular Events Basic to Cellular Radiation Response. Available from National Technical Information Service, Springfield, VA, as DE81027890, 23 pp., 1981.**

The initiation and control of the division process in normal cells is studied to gain insight into changes in these regards caused by x-irradiation and neoplasia. The Primer Hypothesis for eukaryotic gene regulation proposes that small molecular weight RNA acts as primer for new RNA synthesis by hybridizing with DNA and there initiating the transcription of a new RNA chain. The experiments reported here indicate that small molecular weight RNA will induce the production of new proteins. These results are consistent with the Primer Hypothesis, and demonstrate that RNA can be taken up from the media by cells in culture and can induce in vitro the production of differentiated cell products. (Author abstract)

## ENVIRONMENTAL RADIATION AND PROTECTION STANDARDS

### 26. HEALTH EFFECTS OF RADON FROM COAL BURNING.

**Cohen BL**
**Dept. Physics and Astronomy, Univ. Pittsburgh, Pittsburgh, PA. 15260**
**Health Phys; 42(5):725-727 1982**

The number of fatalities resulting from radon emission during coal burning was examined. It was concluded that coal burning will eventualy cause 30 fatalities/GWe-yr through radon emission. It was suggested that based on the number of predicted fatalities, coal burning is 180x more harmful than the radioactive waste from nuclear energy. If radon effects are included in the latter, nuclear energy becomes a net life saver of impressive proportions. (8 Refs)

### 27. ENVIRONMENTAL RADIATIONS AND CHILDHOOD DYNAMIC STATISTICS.

**Sakka M**
**Tohoku Univ. Sch. Medicine, Sendai, Miyagi Prefecture, Japan**
**Nippon Igaku Hoshasen Gakkai Zasshi; 41(10):1004-1008 1981**

In Fukushima prefecture the first nuclear power plant attained criticality in 1971. Since then six reactors have been in operation. Increasing concern is the possible adverse effects due to ionizing radiations released from nuclear reactors. As the radiation level around the nuclear power plants is usually low, induced effects are necessarily delayed ones which require tens of yr to appear. Among other tissues, embryos and fetuses are most radiosensitive and induced effects result in the change of childhood dynamic statistics. In this report dynamic statistics including stillbirth, perinatal death, neonatal death, infant death, 3rd yr examinations were surveyed in 18 health centers in the prefecture from 1961 to 1979. Environmental radiation levels in each district (health centers) were compared and were arranged in order. Dynamic statistics were also compared for each district and were arranged in order. Order correlation coefficients were calculated and a linearity between radiation level and health status was tested. No significant values were obtained ranging from 0.66 to-0.43 of correlation coefficients. Still birth decreased 4.4%/y since 1963 and neonatal death decreased 6.7%/y and infant death also decreased 8.7%/y since 1957 on an av. These decreases were negatively correlated with the proliferation of water supply service, sewage service and increase of physicians in 18 districts including 2 which are under continuous observation of environmental radiations released from nuclear power plants. Childhood dynamic statistics have been turning better in the last 10 yr in prefecture with the difference of 47 mR/y (lowest values of 56 mR/y on an av in 3 prefectures and highest of 103 mR/y in 4). Environmental radiation may initiate adverse effects on prenatal lives but the hygienic improvement in recent yr must extinguish the promotion of the adverse effects. This may be a plausible explanation. (Author abstract) (9 Refs) (In JPN)

### 28. IDENTIFYING THE HEALTH RISKS FROM VERY LOW-DOSE SPARSELY IONIZING RADIATION.

**Dreyer NA, Friedlander E**
**Epidemiology Resources, Inc., P.O. Box 57, Chestnut Hill, MA, 02167**
**Am J Public Health; 72(6):585-588 1982**

The health risks from low-dose sparsely ionizing (low-LET) radiation have been the subject of continued debate. At present, quantitative estimates of risk are extremely uncertain due to the controversy surrounding both the dosimetry for A-bomb survivor data and the choice of mathematical models for extrapolating risk from high to low doses. Nevertheless, much can be learned about the nature of the health risks by reviewing the epidemiologic literature. We present a summary of diseases which have been associated with low-LET radiation (less than 1,000 rad) in at least two independent studies, according to the mean cumulative organ dose at which the disease was observed. At organ doses of less than or equal to 50 rad, the only diseases that have been reported consistently are thyroid cancer, salivary gland tumors, and leukemia. The first two diseases were observed in association with x-ray epilation of the scalp for tinea capitis, a therapy which is no longer employed. On the other hand, leukemia has been observed repeatedly to occur at cumulative doses greater than or equal to 30 rad low-LET radiation. (Author abstract) (35 Refs)

### 29. SCIENTIFIC STRATEGIES TO SAVE YOUR LIFE.

**Bross ID**
**Roswell Park Memorial Inst. Cancer Research, Buffalo, NY**
**Scientific Strategies to Save Your Life. New York, Marcel Dekker, Inc., Statistics-Textbooks and Monographs, Vol. 35, 259 pp., 1981.**

The public health problems associated with hazardous technological products and processes are discussed, with emphasis on the risks of low-level radiation exposure. Data presented to the Nuclear Regulatory Commission based on results of the Tri-State Survey carried out in areas of upstate New York, Maryland, and Minnesota are considered. Analysis of the incidence of leukemia and indicator diseases in a population base of 13 million persons has shown that the children of persons exposed to low-level radiation have a relative risk of 50 for leukemia and a relative risk of 5 for the indicator childhood disease (asthma, eczema, urticaria, pneumonia, dysentery, or rheumatic fever). Both the linear extrapolation model and the threshold model fail to fit the observed disease counts. These findings are interpreted as an indication that the actual dose-response curve flattens as it approaches the 1-rad range and the extrapolative estimates seriously underestimate the actual risk of the low-level radiation. Public health issues involved in the controversy over low-level radiation include the specification of permissible exposure levels in the nuclear industry and cost-benefit analysis of mass screening programs for breast cancer. A cost-to-benefit ratio of 125:1 is thought to be based on a miscalculation. Propagation of such an error may lead to a serious underestimation of the risk of mammography in women less than 50 yr old. (53 Refs)

### 30. HEALTH RISKS TO DISTANT POPULATIONS FROM URANIUM MILL TAILINGS RADON.

**Swift JJ**
**Div. Criteria and Standards, Office Radiation Programs, Washington, DC**
**Health Risks to Distant Populations from Uranium Mill Tailings Radon. Available from National Technical Information Service, Springfield, VA, as PB82-137811, 40 pp., 1981.**

Uranium mill tailing piles can expose the population to radiation by several pathways. The author believes the air pathway to be the most important and radon-222 to be the principal nuclide. The report illustrates the effects of tailings piles on a variety of local and regional populations, assesses the effects of the tailings on distant populations, and compares EPA methods and results with assessments by others. (Author abstract)

### 31. THE BEHAVIOUR OF URANIUM-233 OXIDE AND URANYL-233 NITRATE IN RATS.

**Cooper JR, Stradling GN, Smith H, Ham SE**
**Natl. Radiological Protection Board, Harwell, Didcot, Oxfordshire, England**
**Int J Radiat Biol; 41(4):421-433 1982**

Uranium-233 oxide (233UO2) and uranyl-233 nitrate (233UO2(NO3)2) in aqueous suspension have been administered to rats by pulmonary intubation. The 233U associated with the fraction of the 233UO2 less than 4 nm in diameter translocates from lungs to blood at the same rapid rate as 233U from 233UO2(NO3)2. Identical reactions with blood plasma and lung fluid were observed whether the 233U was administered as less than 4 nm 233UO2 particles or 233UO2(NO3)2. It is suggested that oxidation of UO2 to UO3 occurs followed by the formation of uranyl ion. In blood plasma, approximately 50% of the 233U is bound to transferrin, 25% to citrate and 25% on bicarbonate. (Author abstract) (31 Refs)

### 32. TAN NOW, PAY LATER?

**Hopkins H**
**No affiliation given**
**FDA Consum; 16(3):9-11 1982**

The short-term and long-term effects of prolonged, excessive exposure to UV radiation are discussed. Such effects include skin blistering and burning, eye injury, premature skin aging, and an increased risk for development of skin cancer. While the fatality rate due to the two most common types of skin cancer (basal cell and squamous cell carcinoma) is low, melanoma has a 40-50% mortality rate. New Food and Drug Administration labeling requirements for sunscreen products (the sun protection factor (SPF) numerical system) are considered. (no Refs)

### 33. ALARA DOSIMETRY STUDY FOR NON PRODUCTIVE RADIATION EXPOSURES IN PACIFIC NORTHWEST LABORATORY FACILITIES.

**Hadlock DE**
**Battelle Pacific Northwest Lab., Richland, WA**
**ALARA Dosimetry Study for Non Productive Radiation Exposures in Pacific Northwest Laboratory Facilities. Available from National Technical Information Service, Springfield, VA, as DE81027838, 21 pp., 1981.**

A special ALARA study was conducted during 1980 in selected Pacific Northwest Laboratory facilities. The study utilized thermoluminescent dosimeters (TLDs) which were designed to detect gamma, beta, and neutron exposures; however, only gamma exposures are evaluated in this report. The processing of ALARA (As Low As Reasonably Achievable) dosimeters was performed by the Dosimetry Technology Section of the Radiological Sciences Department. Evaluation of dosimetry data and locations was performed in conjunction with the Radiation Monitoring Section and the Radiological Safety and Engineering Section of the Occupational and Environmental Protection Department. This study was prompted by a DOE-RL directive to reduce radiation exposure to As Low As Reasonably Achievable (ALARA) with a goal of no personnel whole-body penetrating exposures exceeding 3 rem for calendar year 1980. The purpose of this study was to characterize the background radiation environment at selected locations within PNL facilities. Attention was focused on non productive radiation exposure received from the work environment. (Author abstract)

### 34. STATISTICAL APPROACH TO THE ANALYSIS OF OCCUPATIONAL RADIATION EXPOSURE (MEETING ABSTRACT)

**Breslow N**
**University of Washington, Seattle, WA**
**148th National Meeting of the American Association for the Advancement of Science, January 3-8, 1982, Washington, D.C. American Association for the Advancement of Science 182 pp., 1982.**

In analyzing long term follow-up studies of occupational cohorts, the statistician attempts to relate complicated work histories to the subsequent development of cancer and other diseases, while accounting for the possibly confounding effects of age, calendar period and (when appropriate data are available) personal characteristics. An advantage of studies of radiation workers is that relatively precise quantitative information on exposure levels is often recorded annually. This paper illustrates and compares four methods of analysis of such data, all of which are based on the proportional hazards (PH) survival time model with time-dependent covariates: (1) PH model in conjunction with external standard rates; (2) Partial likelihood analysis of the PH model with unknown standard rates; (3) Case-control analysis with controls sampled at random from the risk sets; (4) Case-control analysis using deaths from 'unrelated' causes as controls. A connection is made between methods (1) and (4) and the well known techniques of standardized mortality ratios (SMR) and proportional mortality ratios (PMR). (no Refs)

### 35. SKIN CANCER/MELANOMA (SC/M) PROFESSIONAL EDUCATION IN HAWAII: AN INTEGRATED APPROACH TO TECHNOLOGY TRANSFER (MEETING ABSTRACT)

**Brannon BR, Yanagisako K, Putnam G**
**Control Program, Cancer Center, University of Hawaii, Honolulu, HI**
**1982 ACCC/Progress in Cancer Control III: Clinical Sessions, 8th National Meeting, March 4-7, 1982, Washington, DC Association of Community Cancer Centers; :AC-3 1982**

The incidence of skin cancer has risen dramatically nationwide in the last 2 decades; and, in Hawaii, the incidence of melanoma among Caucasians has increased sevenfold. UV-B band radiation from the sun is the primary cause of skin cancer and has been implicated in the etiology of melanoma among Caucasians. Technical training slide/tape presentations were designed and implemented in Hawaiii in an effort to reduce morbidity/mortality of the diseases through improved prevention, early detection and appropriate treatment. Target audiences were: 1) primary care physicians, 2) non-medical health professionals (eg, nurses, dentists) and 3) personal services professionals (eg, barbers, beauticians) whose expertise is not primarily health-related but who, in the provision of their services, are afforded regular opportunities to examine client skin. (no Refs)

## REVIEWS AND OTHER STUDIES

### 36. CANCER: A COMPREHENSIVE TREATISE. VOLUME 1. ETIOLOGY: CHEMICAL AND PHYSICAL CARCINOGENESIS. SECOND EDITION.

**Becker FF**
**Univ. Texas System Cancer Center, M.D. Anderson Hosp. and Tumor Inst., Houston, TX**
**Cancer: A Comprehensive Treatise. Volume 1. Etiology: Chemical and Physical Carcinogenesis. Second Edition. New York, Plenum Press, 714 pp., 1982.**

In order to eradicate cancer, carcinogenic agents must be identified and their mechanism of action, understood. Crucial interactions between these carcinogens and important macromolecules within the cell must be identified, and those which relate to carcinogenesis must be distinguished from those which are extraneous. The alterations of cell function induced by these reactions must be examined so that phenotypic variation may be understood and an explanation provided for why malignant cells escape from normal homeostatic control. Malignancy must be defined so that the characteristics of cellular activity that permit the malignant cell to compete so effectively with the normal constituent can be defined. The goals of cancer research in general and of the present text are reflected in chapters on cytogenetics, hormones, immunocompetence, chemical carcinogenesis, metabolism of chemical carcinogens, interactions of carcinogens with nucleic acids, effects of carcinogens on cell organelles, sequential aspects and effects in chemical carcinogenesis, radiation, radiation carcinogenesis, and cancer associated with asbestosis, schistosomiasis, foreign bodies, and scars. (3320 Refs)

### 37. PHYSICAL CARCINOGENESIS: RADIATION - HISTORY AND SOURCES.

**Upton AC**

**Health Sciences Center, State Univ. New York, Stony Brook, NY**

**Cancer - A Comprehensive Treatise Vol. 1. Etiology - Chemical and Physical Carcinogenesis. Second Edition. Becker FF, ed. New York, Plenum Press, 714 pp., 1982.**

Carcinogenic activity has been documented for radiations of the electromagnetic spectrum and for corpuscular, or particulate, radiations. Of the electromagnetic radiations, only UV radiations and the ionizing radiations are known to possess carcinogenic properties, whereas corpuscular radiations which are also ionizing, have been found to be carcinogenic in every case investigated. The carcinogenic effects of UV radiation and of the ionizing radiations are attributed to their production of physicochemical changes in critical macromolecular constituents. Cancers were first noted among early radiologists and radiation workers. Dial painters, miners of radioactive are, Japanese atomic bomb survivors, and natives of the Marshall Islands (who were accidentally exposed to nuclear fallout from a weapon test) are among earlier groups which developed specific types of cancer attributed to radiation exposure. Safety standards established by the Federal Radiation Council stipulated that occupational exposure of the whole body and the most radiosensitive organs of the body should not deliver a cumulative dose (in rems) exceeding 5x the age of the worker (in yr) beyond age 18. (65 Refs)

### 38. BIOPHYSICAL ASPECTS OF RADIATION CARCINOGENESIS.

**Kellerer AM, Rossi H**

**Institut fur Medizinische Strahlenkunde, Univ. Wurzburg, Wurzburg, W. Germany**

**Cancer - A Comprehensive Treatise Vol. 1. Etiology - Chemical and Physical Carcinogenesis. Second Edition. Becker FF, ed. New York, Plenum Press, 714 pp., 1982.**

Radiation is termed 'ionizing' when its interactions are so energetic that they remove electrons from the atoms that constitute the irradiated matter. In the case of many materials - including tissues - this leads to permanent changes that are produced with far greater efficiency than is obtained with radiations that merely induce electronic or molecular excitations. Ionization occurs through the agency of electrically charged particles that may be high-speed electrons or nuclear constituents such as protons and alpha-particles. The principal process determining the range of charged particles is electronic collision. The rate of energy loss of charged particles is known as the linear energy transfer which is only an av. characterizing a complicated process. The track of an ionizing particle consists of primary ionizations produced in close proximity to the geometrical trajectory and secondary ionizations that surround this path up to highly variable distances. The physical quantity which is of central importance in radiobiology is the absorbed dose, and the rad is the unit of absorbed dose. Many radiobiological phenomena and at least one type of radiation carcinogenesis are due to tissue response to radiation injury. Findings on the induction of mammary neoplasms demonstrate a complexity of the process of radiation carcinogenesis that is also reflected in the variety of often complicated dose-effect relations observed in other experimental animal studies. (103 Refs)

### 39. ULTRAVIOLET RADIATION: INTERACTION WITH BIOLOGICAL MOLECULES.

**Urbach F**

**Temple Univ. Sch. Medicine, Skin and Cancer Hosp., Philadelphia, PA**

**Cancer - A Comprehensive Treatise Vol. 1. Etiology - Chemical and Physical Carcinogenesis. Second Edition. Becker FF, ed. New York, Plenum Press, 714 pp., 1982.**

Among the major effects of UV radiation on biological systems are inhibition of cell division, inactivation of enzymes, induction of mutation, and killing of cells and tissues. Some of the biological effects of UV radiation can now be explained in terms of specific chemical and physical changes produced in DNA. Structural defects are produced in DNA by chemical mutagens and by radiations. Three major kinds of DNA recovery have been described. The damaged molecule can be restored to its functional state in situ, or it may be removed and replaced with undamaged material to restore normal function, or it may remain unrepaired, but the cell may either bypass or ignore the damage. Enzyme-catalyzed photoreaction is the best-known form of in situ repair. Excision repair involves recognition, incision, excision and repair replication, and rejoining. Several observations and biological and biochemical studies support the assumption that exposure to sunlight, particularly the mid-UV component, is an essential and major factor in the development of most skin cancers. Skin cancer appears on those parts of the body most exposed to sunlight, particularly the head, neck, arms, and hands. (54 Refs)

### 40. RADIATION CARCINOGENESIS.

**Storer JB**

**Biology Div., Oak Ridge Natl. Lab., Oak Ridge, TN**

**Cancer - A Comprehensive Treatise Vol. 1. Etiology - Chemical and Physical Carcinogenesis. Second Edition. Becker FF, ed. New York, Plenum Press, 714 pp., 1982.**

Ionizing radiation in sufficiently high dosage acts as a complete carcinogen in that it serves as both initiator and promoter. Cancers can be induced in nearly any tissue or organ of man or experimental animals by the proper choice of radiation dose and exposure schedule. Myeloid leukemia and the acute leukemias are probably the most easily induced of all radiation-induced neoplasms. Unlike solid tumors of other tissues with a long latent period, the leukemias occur early, show a high incidence, and then fall close to the control incidence. The other relatively easily induced tumor in human populations is cancer of the thyroid, particularly when the radiation is delivered to juveniles. Breast cancer can also be induced by radiation exposure but higher doses are required for its induction. Evidence that the lung is moderately sensitive to cancer induction is provided principally from studies of uranium miners occupationally exposed to radon. The salivary gland is moderately sensitive to cancer induction, and a few have been reported as being radiation-induced. Cancer of the skin was a frequent sequela to exposure to very large doses of radiation received by earlier x-ray workers who were unaware of the hazards of radiation exposure. Like skin, bone is resistant to cancer induction, even though a large number of radiation-induced sarcomas have been reported. Physical factors that effect carcinogenesis include dose rate, radiation quality, internal emitters vs external exposure, total body and partial body exposure, and host factors. (103 Refs)

### 41. SEQUENTIAL ASPECTS OF CHEMICAL CARCINOGENESIS: SKIN.

**Berenblum I**
**Weizmann Inst. Science, Rehovot, Israel**
**Cancer - A Comprehensive Treatise Vol. 1. Etiology - Chemical and Physical Carcinogenesis. Second Edition. Becker FF, ed. New York, Plenum Press, 714 pp., 1982.**

The two-stage hypothesis, the initiation-promotion hypothesis, was based on animal studies of sequential stages of skin carcinogenesis. Initiators for skin carcinogenesis include 2-acetylaminofluorene, UV light, beta-radiation, certain metabolites of 'complete' carcinogens, various alkylating agents and mutagens. Promoters for skin carcinogenesis include physical agents, 'complete' chemical carcinogens, non- or weakly-acting skin carcinogens, croton oil, straight-chain N-alkanes, phenolic compounds, extracts of tobacco leaf, and extracts of tobacco smoke condensates. The two-stage system in skin carcinogenesis has been extended, based on further experiments. Evidence that a mutational change in the DNA genome was responsible for the initiating change of carcinogenesis is based on the ability of most carcinogens to bind with DNA and that there is a fairly good correlation between mutagenic and carcinogenic properties among a wide range of compounds. Evidence for the stimulation of synthetic processes in the cell includes the stimulation of DNA and RNA synthesis as well as protein and phospholipid synthesis. The effects of enzymatic functions in the cell are based on an increase in proteinase activity, on stimulation of ornithine decarboxylase activity, on changes in cyclic nucleotide levels, and on a decrease in histidase activity. (378 Refs)

### 42. HEALTH EFFECTS OF RADON EMISSIONS FROM URANIUM MILL TAILINGS.

**Cohen BL**
**Univ. Pittsburgh, Pittsburgh, PA, 15260**
**Health Phys; 42(5):695-702 1982**

The problem of health effects of radon emissions from uranium mill tailings is reviewed. The history of estimates of these effects and how they have been refined by further research is traced, and a current best estimate is given. The theory and practice of mitigating the effects by covering tailings with soil are described, and the present situation as regulated by the new 10 CFR 40, Appendix A is evaluated. (Author abstract, (29 Refs)

### 43. ETIOLOGY OF MOUTH AND LIP TUMORS.

**Zabezhinskii MA, Gogotouzha PD**
**N. N. Petrov Res. Inst. Oncology, Leningrad, USSR**
**Vopr Onkol; 28(2):105-113 1982**

Literature data on the etiology of mouth and lip cancers are reviewed. Pathogenesis of mouth neoplasms is associated with the exposure to various chemical, physical, and biological carcinogenic factors alone or in combination with the modifying factors. The increased incidence of mouth cancer can be caused by smoking, tobacco chewing, exposure to polycyclic aromatic hydrocarbons, alcohol consumption, and exposure to pesticides. Physical carcinogens include UV, x rays, and sunlight. Experimental data indicate that herpes virus and polyoma virus can induce adenomas and adenocarcinomas of mouth mucosa. Poor hygiene of the mouth can increase the risk of development of mouth cancer. Chronic irritation of the mouth mucosa was shown to enhance penetration of carcinogens into mucosa and to stimulate cell proliferation. Bacterial flora of the oral cavity was shown to contribute to the metabolism of chemical carcinogens. Deficiency of vitamins A and B led to development of precancerous conditions of the mouth mucosa. (74 Refs) (In RUS)

### 44. PHOTOREACTIONS OF THE SKIN.

**Jung EG**
**Hautklinik, Klinikum der Stadt Mannheim, Postfach 23, D-6800 Mannheim, W. Germany**
**Ther Umsch; 39(3):156-162 1982**

Clinical implications of reactions of the skin to light are reviewed. Light affects cellular molecules primarily by acting on electrons in high-energy orbitals. Physiological effects of exposure to UV include early effects (such as sunburn) and late effects (such as carcinogenesis). UV induces carcinogenesis by producing reversible and irreversible damage to DNA in the form of thymine dimers. (7 Refs) (In GER)

### 45. SIGNIFICANCE OF ENVIRONMENTAL FACTORS FOR THE DEVELOPMENT OF LEUKEMIA, MYELOMA AND MALIGNANT LYMPHOMA.

**Brandt L**
**Onkologiska kliniken, Lasarettet, Lund, Sweden**
**Lakartidningen; 79(15):1490-1492 1982**

Studies on environmental factors in the etiology of leukemias, myelomas and lymphomas are reviewed. Ionizing radiation plays a role in the development of acute myeloid leukemia, acute lymphocytic leukemia, chronic myeloid leukemia, myeloma, Hodgkin's disease and non-Hodgkin's lymphomas, but probably none in chronic lymphocytic leukemia. Viral etiology of chronic lymphocytic leukemia in farm workers and of Burkitt's lymphoma and of other non-Hodgkin's lymphomas is suspected. Hodgkin's disease was found to be overrepresented among men exposed to chemicals. (35 Refs) (In SWE)

### 46. ENVIRONMENTAL FACTORS AND MALIGNANT HEMATOLOGICAL DISEASES.

**Bjorkholm M**
**Hematologsektionen, Danderyds sjukhus, Danderyd, Sweden**
**Lakartidningen; 79(15):1457-1459 1982**

Environmental factors and their possible or demonstrated etiological role in malignant hematological diseases are reviewed. Ionizing radiation is a well-established cause of leukemia, but no relationship between exposure to such radiation and chronic lymphocytic leukemia was found. Benzene is considered as a leukemogenic factor, even though it was not possible to induce leukemia with benzene in experimental animals. Environmental factors during childhood may play a role in the development of Hodgkin's disease. (44 Refs) (In SWE)

### 47. HIGH RISK FACTORS IN LUNG CANCER.

**Valentino B, Vigorito F, Lepparelli G, Moscariello E, Leita L, Valentino D**
**III Divisione di Pneumologia, Ente Ospedaliero 'V. Monaldi', Napoli, Italy**
**Rass Int Clin Ter; 61(16):1105-1113 1981**

Risk factors in pulmonary cancer were discussed including occupational factors, air pollution, smoking, radiation, sex, and age. Changes induced in respiratory passages by different environmental factors and diseases and their synergistic action were considered. (35 Refs) (In ITA)

### 48. CHROMOSOMES, CANCER, AND RADIOSENSITIVITY (MEETING ABSTRACT)

**Samouhos E**
**Radiation Therapy Service, Veterans Administration Medical Center, Martinez, CA, 94553**
**Am J Clin Oncol; 5(2):136 1982**

Some specific chromosomal abnormalities are associated with certain cancers. The earliest description of such a specific association is that of the Philadelphia chromosome and myelogenous leukemia (1960). Other congenital karyotype abnormalities are associated with specific cancers. Examples are Down's syndrome with leukemia and Klinefelter's syndrome with male breast cancer. Genetic diseases of increased chromosome breakage, or of defective chromosome repair, are associated with greatly increased cancer incidence. Three such diseases have been recognized: 1) Fanconi's anemia, associated with leukemias and lymphomas; 2) Bloom's syndrome, associated with acute leukemias and lymphosarcoma; and 3) ataxia telangiectasia, associated with Hodgkin's disease, leukemia and lymphosarcomas. Ten percent of individuals with ataxia telangiectasia will develop one of these neoplasms. Individuals with certain of these syndromes display an unusually high radiosensitivity. Radiation therapy for cancer has been fatal in patients who received as little as 3000 rad. This remarkable radiosensitivity has been quantitated in cell cultures from such cases. Evidence suggests that the apparent sensitivity may reflect subnormal ability to repair radiation damage. (no Refs)

### 49. RADIOBIOLOGY OF RISK ESTIMATES IN MEDICAL IRRADIATION (MEETING ABSTRACT)

**Rossi HH**
**Columbia University, New York, NY**
**IN: 148th National Meeting of the American Association for the Advancement of Science, January 3-8, 1982, Washington, D.C American Association for the Advancement of Science 182 pp., 1982.**

Intensive efforts to determine the effects of ionizing radiation on human health have yielded approximate information on cancer and genetic hazards for doses that are of the order of 1 Gy (100 rad). Although there are important data for considerable numbers of Japanese A-bomb survivors exposed to somewhat lower doses, the magnitudes of these doses (as well as the nature of the radiation involved) are currently uncertain. Estimates of the risk attendant to procedures in diagnostic radiology must therefore be based on extrapolations to doses that are at least one, and more typically two or three, orders of magnitude lower than those for which we have reasonably reliable knowledge. The radiobiological considerations that may serve as a guide for such extrapolations will be critically reviewed. (no Refs)

### 50. THE ROLE OF A-BOMB SURVIVOR STUDIES (MEETING ABSTRACT)

**Land CE**
**National Cancer Institute, Bethesda, MD**
**148th National Meeting of the American Association for the Advancement of Science, January 3-8, 1982, Washington, D.C. American Association for the Advancement of Science 182 pp., 1982.**

The estimated risk of radiation-induced cancer from medical diagnostic radiation procedures, which are in general given at low radiation doses, is derived from observations on populations with histories of high-dose exposures. These populations include patients given radiation therapy or exposed to high-dose diagnostic radiation, groups with higher-level occupational exposures, and the survivors of the atomic bombs dropped on Hiroshima and Nagasaki. Consistency among estimates obtained from different populations is the most important single criterion for reliability of these estimates. Currently, there are questions about the estimates based on the most important data source, the A-Bomb survivor studies, because of uncertainties about the dosimetry currently in use for these studies. The implications of these uncertainties for risk estimation are discussed. (no Refs)

### 51. RADIATION CARCINOGENESIS: PROBLEMS OF RISK ESTIMATION (MEETING ABSTRACT)

**Land CE**

**National Cancer Institute, Bethesda, MD**

**148th National Meeting of the American Association for the Advancement of Science, January 3-8, 1982, Washington, D.C. American Association for the Advancement of Science 182 pp., 1982.**

The quantification of cancer risk associated with exposure to low doses of ionizing radiation is a substantial problem with urgent practical consequences as well as extensive implications for carcinogenesis in general. The utility of direct, straightforward approaches to the problem based on observation of populations with low-dose exposures is severely limited by considerations of bias and sample size. This necessitates a more sophisticated indirect approach directed toward the testing, modification, and refinement of general theories of radiation carcinogenesis. (no Refs)

### 52. RADIATION EPIDEMIOLOGY (MEETING ABSTRACT)

**Marks S**
**No affiliation given**
**148th National Meeting of the American Association for the Advancement of Science, January 3-8, 1982, Washington, D.C. American Association for the Advancement of Science 182 pp., 1982.**

The field of radiation epidemiology has concerned itself with the collection and analysis of data on human populations exposed to radiation as a result of (1) medical radiation therapy for specific diseases, (2) occupation, and (3) atomic bombings of the Hiroshima and Nagasaki populations. Having demonstrated the causal relationship of radiation to human cancer, the activities of greatest interest in carrying out current studies are the identification of specific cancer types attributable to radiation in these populations and the development of dose-response relationships. The latter may differ for various types of radiation and exposure patterns. Biostatisticians must carry out procedures to characterize statistically significant relationships between radiation exposure and cancer types, establish appropriate dose-response relationships and estimate parameter values. The epidemiologist collects and elevates the data on exposure and health effects. Important studies in the three major exposure categories will be reviewed briefly in this paper, and generic and special problems in the relevant sets of exposure and health data discussed. (no Refs)

### 53. CANCER ETIOLOGY: CURRENT STATES OF OUR KNOWLEDGE (MEETING ABSTRACT)

**Thomas DB**
**No affiliation given**
**Fifth Annual Snohomish County Cancer Conference, February 11, 1982, Everett, Washington Snohomish County Medical Education Board; 1982**

The environmental causes of cancer (known and suspected) are: A) chemicals - tobacco smoke, alcohol, industrial exposures, and drugs; B) radiation - ionizing and non-ionizing; C) exogenous hormones - transplacental exposures, oral contraceptives, menopausal estrogens, and others; D) infectious agents - viruses and others; and E) dietary factors - deficiencies, excesses, and contaminants. (no Refs)

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As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

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# ICRDB CANCERGRAM

# RADIATION CARCINOGENESIS

SERIES CK06 No. 82/11

NOVEMBER, 1982

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## RADIATION CARCINOGENESIS IN HUMANS

### 1. DELAYED EFFECTS OF A-BOMB RADIATION: A REVIEW OF RECENT MORTALITY RATES AND RISK ESTIMATES FOR FIVE-YEAR SURVIVORS.

**Stewart AM**
**Cancer Epidemiology Res. Unit, Dept. Social Medicine, Univ. Birmingham, Edgbaston, Birmingham B15 2TT, England**

**J Epidemiol Community Health; 36(2):80-86 1982**

A general conclusion generated by the published data of mortality and morbidity of atomic-bomb survivors is that since they were based on the mortality experiences of 5-yr survivors, estimates of radiation effects were controlled for the two opposing forces of selective survival of exceptionally healthy persons and residual disabilities. The question that should be considered is why the change from the very high death rate of the first 6 mo to the near normal rate of the 1950's was not accompanied by a change from a positive to a negative association with dose. Differences in death rates in Nagasaki and Hiroshima are discussed. The group of blood diseases, with aplastic anemia as its main component, is the only diagnostic group studied with an increased and dose-related death rate. Past

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studies have been obsessed with possible mutational effects of ionizing radiation to the exclusion of all else, even though it is known that the threshold for bone marrow damage is relatively low and that aplastic anemia is the most easily recognized effect of such damage. The two opposing forces explain why the change from high mortality rates of 1945-1946 to low rates in the 1950's was not accompanied by a change from a positive to a negative association with dose. Imperviousness to the residual disabilities may be the reason why sudden deaths of previously healthy individuals (exemplified by suicides) were an exception to the rule. An early epidemic of myeloid leukemia, the apparent absence of other cancers at this time and the relatively high dose-related death rates for blood diseases other than leukemia are probably the result of impairment of bone marrow function. (21 Refs)

### 2. MYXOID LIPOSARCOMA OF THE URINARY BLADDER (MEETING ABSTRACT).

Kropfl D, Richter HJ, Ringert RH, Homann W
Urologische Klinik und Pathologisches Institut, Klinikum der, Gesamthochschule Essen Hufelandstr 55, 4300 Essen 1, W. Germany
28 Tagung der Nordrhein-Westfalischen Gesellschaft fur Urologie, May 6-8, 1982, Krefeld, W Germany Nordrhein-Westfalischen Gesellschaft fur Urologie; 1982

Bladder sarcoma is quite rare in adults making up less than 1% of bladder tumors. Twenty-seven yr after primary irradiation for carcinoma of the cervix our patient developed a tumor of the bladder. The tumor, identified as a liposarcoma myxoides rapidly recurred despite repeated transurethral resections. Cystectomy and urinary diversion were performed. The operation was not radical. The postoperative course was complicated by a small intestine-skin and small intestine-vaginal fistula. The patient underwent laparotomy 6 mo later for small intestine ileus. The entire lower abdomen and part of the small intestine were imbedded in the tumor mass. The patient died in the immediate postoperative period. Problems of diagnosis and rational treatment of this rare bladder tumor are discussed together with its possible etiology as a second tumor following radiation therapy. (no Refs) (In GER)

### 3. CHEST FLUOROSCOPY AND NEOPLASIA IN TUBERCULOSIS PATIENTS: A RETROSPECTIVE SURVEY. FINAL REPORT.

Battigelli MC, Wood WB
Sch. Medicine, North Carolina Univ. at Chapel Hill, Chapel Hill, NC
Chest Fluoroscopy and Neoplasia in Tuberculosis Patients: A Retrospective Survey. Final Report. Available from National Technical Information Service, Springfield, VA, as DE82003354, 156 pp., 1981.

An historical cohort study has been conducted to assess the risk for cancer associated with exposure to fluoroscopic radiation, pulmonary tuberculosis. On the basis of an estimated 30,000 patient population admitted to the three sanatoria of the State of North Carolina between 1930 and 1955, individual records were analyzed at McCain State Sanatorium (NCS), at Western North Carolina Sanatorium (WNCS) and at Eastern North Carolina Sanatorium (ENCS). In terms of general mortality, the category of all deaths indicated an excess in the group with the highest exposure. Age-standardized proportional mortality analysis has revealed a moderate relative excess of cancer deaths occurring, in the exposed population, at least 15 years after initial exposure. This lapse of time was computed from the first fluoroscopic examination, on the basis of an assumed minimal latency of 15 years. Through a life-table analysis, death rates (al) were assessed and relative risk estimated for this population exposed to repeated fluoroscopy, in relation to the mortality experienced by the North Carolina reference population. Relative risk was found to be greatest for white males in the NCS (RR = 6.13) and WNCS (RR = 3.83). All of these deaths occurred in patients who received more than 100 fluoroscopic exposures. (Author abstract)

## EXPERIMENTAL RADIATION CARCINOGENESIS

### 4. SIMULATED STRATOSPHERIC OZONE DEPLETION AND INCREASED ULTRAVIOLET RADIATION: EFFECTS OF PHOTOCARCINOGENESIS IN HAIRLESS MICE.

Forbes PD, Davies RE, Urbach F, Berger D, Cole C
Center for Photobiology, Temple Univ. Sch. Medicine, Skin and Cancer Hosp., 3322 North Broad St., Philadelphia, PA, 19140
Cancer Res; 42(7):2796-2802 1982

Solar ultraviolet radiation at the surface of the earth is a recognized cause of skin cancer. Postulated anthropogenic reductions in the thickness of the ozone layer would lead to an increased amount of ultraviolet radiation and hence would be expected to increase the risk of skin carcinogenesis. This study uses hairless (Skh:HR) mice as an animal model to study this increased risk. The mice were exposed 5 days/wk to graded doses of ultraviolet radiation from a xenon arc lamp attenuated by five different thicknesses of Schott glass filters (WG320) to simulate various ozone layer thicknesses. A Robertson-Berger sunburning ultraviolet meter was used as one of the forms of dosimetry. The results of the various exposure treatments are expressed as the percentage of animal with tumors (incidence) versus time after commencing irradiation and as cumulative tumor yield (average number of tumors per survivor) versus time time. With any given filter, the time to 50% incidence is inversely related to daily dose in Robertson-Berger meter units. The time to 50% incidence for comparable Robertson-Berger meter doses through different filter thicknesses increases with increasing thickness. These results indicate that the effective dose for skin cancer induction may be estimated from the Robertson-Berger meter dose but that the Robertson-Berger meter response spectrum underestimates the photocarcinogenic effectiveness of the shorter wavelengths. The cumulative tumor yield data are also consistent with these conclusions. Alternate weighting of the source spectra with the acute-response action spectrum for mouse skin edema gave a better correlation between unit dose and time to a tumor response, independent of the source spectral distribution. This suggests that the mouse skin edema action spectrum, indistinguishable from a human skin erythema action spectrum for lambda greater than 295 nm, is similar in shape to the mouse skin photocarcinogenesis action spectrum for lambda greater than 295 nm. (Author abstract) (18 Refs)

### 5. LUNG CARCINOGENESIS DURING IN VIVO CIGARETTE SMOKING AND RADON DAUGHTER EXPOSURE IN RATS.

Chameaud J, Perraud R, Chretien J, Masse R, Lafuma J
COGEMA, Service Medical du Travail, Laboratorie de Pathologie Experimentale, BP n 1, F-87640 Razes, France
Recent Results Cancer Res; 62:11-20 1982

The synergistic effects associated with cigarette smoking occuring concomitant with radon exposure, as would occur in uranium miners who use tobacco products, was investigated.

Synergism was demonstrated in Sprague-Dawley rats exposed to cumulative doses of radon and its daughters of 4,000 or 500 work level mo, followed by inhalation of cigarette smoke. The number of tumors occurring in animals treated with both agents was significantly increased as compared to those treated with either agent alone, and tumors which developed were more invasive and metastatic. Histological type of tumor, however, was not altered by tobacco. Preliminary results from new experiments indicate no synergistic effect when smoke inhalation precedes exposure to radon, while delayed exposure to smoke after inhalation of radon resulted in high incidence of tumors. The relationship of these results to epidemiological data obtained in uranium miners is briefly discussed. (12 Refs)

### 6. ACCELERATED DEVELOPMENT OF SPONTANEOUS AND BENZOPYRENE-INDUCED SKIN CANCER IN MICE EXPOSED TO 2450-MHZ MICROWAVE RADIATION.

Szmigielski S, Szudzinski A, Pietraszek A, Bielec M, Janiak M, Wrembel JK
Dept. Biological Effects Non-ionizing Radiation, Center for Radiobiology and Radioprotection, 128 Szaserow, 00-909 Warsaw, Poland
Bioelectromagnetics; 3(2):179-191 1982

Microwave (MW; 2,450-megahertz) treatment for 1-6 mo. of C3H/HeA (CA) mice with high incidence of spontaneous breast cancer and of Balb/c mice with skin cancer induced with topical benzo(a)pyrene (BP), resulted in significant acceleration of tumors. Mice were exposed to MWs in an anechoic chamber at 5 or 15 milliwatts (mW)/square cm (cm2) 2 hr/day x 6/wk. CA mice were irradiated from wk 6 of life up to mo 12. Balb/c mice treated with BP were irradiated either prior to (over 1 or 3 mo) or simultaneously with BP treatment (over 5 mo). Two additional groups were exposed to chronic stress (caused by confinement) or to sham-irradiation; these groups served as controls. The acceleration of tumor growth was accompanied by lowering of the natural antineoplastic resistance as measured by the number of cancer colonies in the lung, which occurred whether MWs were applied before or simultaneous with BP. The acceleration of cancer development in all tested systems and lowering of antineoplastic resistance was similar in mice exposed to MW at 5 mW/cm2 or to chronic stress but differed significantly from the data obtained on animals exposed at 15 mW/cm2, where local thermal effects ('hot' spots) were possible. It is concluded that under the tested experimental conditions, long-term exposure to MW fields may be a potential carcinogenic risk factor. (15 Refs)

## EXPERIMENTAL RADIATION MUTAGENESIS

### 7. EXTENT OF EXCISION REPAIR BEFORE DNA SYNTHESIS DETERMINES THE MUTAGENIC BUT NOT THE LETHAL EFFECT OF UV RADIATION

Konze-Thomas B, Hazard RM, Maher VM, McCormick JJ
(c/o Maher) Carcinogenesis Lab. Fee Hall, Michigan State Univ., East Lansing, MI, 48824
Mutat Res; 94(2):421-434 1982

Predictions that excision repair-proficient cells treated just prior to S will be significantly more sensitive to the cytotoxic and/or mutagenic effect than will be cells exposed many hr prior to S and that cells which are incapable of excision repair will show no difference in sensitivity were tested. Results obtained with UV radiation as the DNA-damaging agent indicated that semi-conservative DNA synthesis is indeed, the 'critical cellular event' responsible for mutation induction. However, the cytotoxic effect of the agent was not significantly increased in normal fibroblasts treated just prior to S phase, even though the cells' excision repair capacity was critical in determining the survival level ultimately attained. (26 Refs)

### 8. EFFECT OF SPLIT DOSES OF RADIATION ON MUTATION FREQUENCY IN RODENT CELL LINES.

Radner BS, Aebersold PM, Kennedy AR
Lab. Radiobiology, Dept. Physiology, Harvard Univ., Sch. Public Health, Boston, MA, 02115
Mutat Res; 94(2):397-403 1982

Cellular mutagenesis resulting from combinations of UV and x-ray exposures and intervals between radiation doses not reported previously were investigated for the existence of an inducible error-prone repair system in mammalian cells which could affect the opinions about the potential hazards involved with fractionated radiation exposures. Data showed that mutation frequencies in C3H/10T1/2 and Chinese hamster V79 cell lines were unaffected by splitting the doses of radiation. The two rodent cell lines used are partially deficient in the excision repair pathway which may account for the observed results. (16 Refs)

## EFFECTS OF IRRADIATION ON CHROMOSOMES AND DNA

### 9. MECHANISMS FOR CHROMOSOMAL ABERRATIONS IN MAMMALIAN CELLS.

Natarajan AT, Zwanenburg TSB
Dept. Radiation Genetics and Chemical Mutagenesis, State Univ. Leiden, Wassenaarseweg 72, 2333 AL Leiden, The Netherlands
Mutat Res; 95(1):1-6 1982

Lesions responsible for chromosomal aberrations (CA) induced by ionizing radiations, role of base damage in x-ray-induced CA, and experiments involving repair inhibitors are discussed. The frequencies of DNA-double strand breaks induced by x-rays alone, as well as in combination with Neurospora crassa endonuclease (NE) were measured by neutral sucrose-gradient centrifugation analysis to confirm the cytological findings and their interpretation. X-irradiation of CHO cells with 30 kilorad led to 8.8 double-strand breaks/10(10) dalton of DNA, and post treatment of the cells with NE led to a doubling of the frequencies of double-strand breaks induced by x-rays supporting the conclusion that DNA double-strand breaks are the most probable lesions that lead to the formation of CA induced by ionizing radiations. When G0 or G1 cells from patients with ataxia telangiectasia were irradiated with x-rays, both chromosome and chromatid types of aberration were obtained in contrast to mainly chromosome-type aberrations obtained in normal cells. Several inhibitors of DNA synthesis, such as cytosine arabinoside, aphidicolin, and hydroxyurea, as well as inhibitors of poly(ADP-ribose) polymerase (PRP), have been used in x-ray experiments involving human peripheral blood lymphocytes. When human peripheral blood lymphocytes were irradiated and post treated with inhibitors of PRP, such as 3-aminobenzamide for at least 6 hr prior to stimulation, a doubling of the frequency of aberrations was observed. The results supported the conclusion that DNA double-strand breaks are the most important lesions responsible for radiation-induced CA. (19 Refs)

### 10. NORMAL SISTER CHROMATID EXCHANGE FREQUENCY IN LONG-TERM SURVIVORS WITH ACUTE LEUKEMIA.

**Inoue S, Brown L, Ravindranath Y, Ottenbreit MJ**
**Children's Hosp. Michigan, Detroit, MI, 48201**
**Cancer Res; 42(7):2906-2908 1982**

We hypothesized that the sister chromatid exchanges assay in acute leukemia long-term survivors may detect: (a) long-term effects of combined chemo- and radiotherapy; and possibly (b) those individuals with inherently deficient DNA repair. Accordingly, we determined the sister chromatid exchanges frequency in 26 blood specimens from 24 acute leukemia long-term survivors (patients) and 14 blood specimens from 13 control subjects (controls). The patients consisted of 23 children with acute lymphocytic and one child with acute myelocytic leukemia. The median length of chemotherapy was 5 years. Eighteen of the 24 patients also received prophylactic fractional central nervous system irradiation for the first 3 years of treatment, and one patient received therapeutic irradiation to the central nervous system. The median off-therapy period at the time of study was 2.5 years with a range of 0 to [illegible].5 years. The controls consisted of the parents of the patients and laboratory personnel. A mean exchange score per cell was established for each specimen (25 to 30 cells/specimen were scored), and it ranged from 3.0 to 9.7 in the patients and from 3.0 to 11.5 in the controls. A mean +- S.D. calculated from those means was 6.0 +-1.8 for the patients and 5.9 +-2.8 for the controls. They were not significantly different. We conclude that chemo- and radiotherapy produced no persistent DNA alterations detectable by this method. (Author abstract) (20 Refs)

### 11. KINETICS OF INDUCTION OF SISTER-CHROMATID EXCHANGES BY X-RAYS THROUGH TWO CELL CYCLES.

**Renault G, Gentil A, Chouroulinkov I**
**Institut de Recherches Scientifiques sur le Cancer, B.P. No. 8, 94802 Villejuif Cedex, France**
**Mutat Res; 94(2):359-368 1982**

Sister chromatid exchange (SCE) induction by x-rays delivered at various times during the two cell cycles needed to obtain harlequin-stained chromosomes (metaphases II) was studied in V79 Chinese hamster cells that were allowed to incorporate 5-bromo-2'-deoxyuridine (BrdUrd) for only 6 hr during the first cell cycle. A linear dose-response was obtained when the x-irradiation was performed just prior to the BrdUrd addition. When the x-irradiation was performed during the first cell cycle the number of SCE progressively increased, and then reached a plateau during the BrdUrd incorporation. The kinetics of SCE induction with N-methyl-N'-nitro-N-nitrosoguanidine was different: no increase was observed during the first cell cycle, and the SCE frequency significantly decreased with the completion of the S phase of both the first and the second cell cycles. After the addition of BrdUrd, the G1 phase appeared first and the G2 phase appeared at the end. The cell cycle was longer for the x-irradiated cells than that for the unirradiated controls, and at the ordinate of 50% tritium-labeled metaphases II, the S phase duration was 7.5 hr for the former and 6.5 hr for the latter. While the number of dicentric chromosomes decreased when cells passed from G1 to S, the frequency of chromosomal aberrations remained stable until the late S phase and a small decrease was observed in G2. The chromatid-type aberration frequency was enhanced by a factor of 3 between G1 and early-middle S. Approx 25% of the cells showed no aberration when x-irradiation was performed prior to the S phase. (16 Refs)

### 12. ULTRAVIOLET-INDUCED CHROMATID EXCHANGES IN V-79 CELLS WITH NORMAL AND BRDURD-SUBSTITUTED DNA AND THE INFLUENCE OF INTERCALATING SUBSTANCES AND CYSTEINE.

**Speit G, Mehnert K, Wolf M, Vogel W**
**Abteilung Klinische Genetik, Universitat Ulm, D-7900 Ulm, W. Germany**
**Radiat Res; 90(3):538-546 1982**

The effect of UV irradiation on the sister chromatid exchange (SCE) frequency of bromodeoxyuridine (BrdUrd)-substituted DNA of V-79 cells was investigated. Cysteine (10(-3) M) did not influence UV-induced SCE frequency of unsubstituted DNA. Cysteine did cause a slight but statistically significant reduction of UV-induced SCEs in BrdUrd-substituted DNA. Since postirradiation treatment with cysteine also led to a reduction in SCE frequency, reactions other than sulfhydryl radical scavenging appeared to be at work. Proflavine (5 x 10(-6) M) did not produce a change in SCE frequency in controls or irradiated cells with unsubstituted DNA. At 10(-5) M, proflavine increased SCE frequency in these cells and in cells containing substituted DNA. These results indicate that the induction of chromosome aberrations or SCEs by UV light in BrdUrd-substituted DNA occur independently and that UV-induced single-strand breaks are more involved in the induction of chromosome aberrations and contribute to the formation of SCEs. (26 Refs)

### 13. ENHANCED YIELD OF CHROMOSOMAL ABERRATIONS IN HUMAN PERIPHERAL LYMPHOCYTES IN VITRO USING CONTRAST MEDIA IN X-IRRADIATION.

**Hadnagy W, Stephan G. Kossel F**
**Institut fur Strahlenhygiene des Bundesgesundheitsamt, Ingolstadter Landstrasse 1, D-8042 Neuherberg, W. Germany**
**Mutat Res; 104(4/5):249-254 1982**

Data on the mechanism for enhancement of chromosomal aberrations in human peripheral lymphocytes in vitro by contrast media in x-irradiation are presented. The absorbed radiation dose in blood containing contrast medium was calculated on the basis of dose-enhancement factors. Blood from healthy donors was treated with contrast medium only, x-rays only, or x-rays with contrast medium added to blood prior to irradiation. Contrast medium combined with x-rays increased radiation-induced chromosomal aberration yield, depending on the iodine concentration; the effect was the result of enhancement of radiation dose due to the photoelectric effect of iodine. (8 Refs)

### 14. EFFECT OF LONG-WAVE ULTRAVIOLET RADIATION ON CYCLOPHOSPHAMIDE-INDUCED INCIDENCE OF CHROMOSOME ABERRATIONS IN MOUSE BONE MARROW CELLS.

**Zhurkov VS, Il'in VP, Prokopenko IuI**
**Inst. General and Community Hygiene, Moscow, USSR**
**Tsitol Genet; 16(2):4-9 1982**

To evaluate the effect of long-wave UV radiation on the yield of cyclophosphamide (CP)-induced chromosome aberrations in the bone marrow, random-bred albino male mice were subjected over a period of 1 mo to irradiation at 0.5 or 3 erythema doses, followed by five intragastric administrations of CP at 0.2-27 mg/kg. The irradiation at 3 erythema doses, but not at the 0.5 erythema dose, increased the incidence of CP-induced chromosome aberrations in the bone marrow cells. (14 Refs) (In RUS)

### 15. IN VITRO EFFECT OF PULSE IONIZING RADIATION ON HUMAN BLOOD LYMPHOCYTES.

**Stiazhkina TV, Khaimovich TI**
**No affiliation given**
**Med Radiol (Mosk); 27(5):68-69 1982**

Cultured human peripheral blood lymphocytes were subjected to 60Co gamma irradiation (50-560 rads) or to Bremsstrahlung irradiation (30-550 rads). The yield of chromosome aberrations after pulse irradiation did not differ from that after continuous irradiation. (4 Refs) (In RUS)

### 16. 'WASTED,' A NEW MUTANT OF THE MOUSE WITH ABNORMALITIES CHARACTERISTIC OF ATAXIA TELANGIECTASIA.

**Shultz LD, Sweet HO, Davisson MT, Coman DR**
**Jackson Lab., Bar Harbour, ME, 04609**
**Nature; 297(5865):402-404 1982**

Pathological changes similar to those of ataxia telangiectasia, found in the CNS and lymphoid system of mutant mice (HRS/J mice backcrossed to C57BL/6J mice), are described. Homozygosity for the wasted mutation results in impaired neurological and immunological development, as well as increased levels of spontaneous and gamma ray-induced chromosomal damage The relationship of the chromosomal aberrations to defective DNA repair is discussed. (11 Refs)

### 17. FAMILIAL MELANOMA ASSOCIATED WITH DOMINANT ULTRAVIOLET RADIATION SENSITIVITY.

**Ramsay RG, Chen P, Imray FP, Kidson C, Lavin MF, Hockey A**
**(c/o Kidson) Queensland Inst. Medical Res., Brisbane 4006, Australia**
**Cancer Res; 42(7):2909-2912 1982**

Sensitivity to ultraviolet radiation was studied in lymphoblastoid cell lines derived from 32 members of two families with histories of multiple primary melanomas in several generations. As assayed by colony formation in agar or by trypan blue exclusion following irradiation, cellular sensitivity showed a bimodal distribution. All persons with melanoma or multiple moles were in the sensitive group, while some family members exhibited responses similar to those of controls. Cells from four cases of sporadic melanoma showed normal levels of sensitivity. The data are consistent with a dominantly inherited ultraviolet light sensitivity associated with these examples of familial melanoma. Spontaneous and ultraviolet light-induced sister chromatid exchange frequencies were similar to those in control cell lines. No defect in excision repair was detected in any of the above cell lines, but the sensitive group showed postirradiation inhibition of DNA replication intermediate between controls and an excision-deficient xeroderma pigmentosum cell line. (Author abstract) (25 Refs)

### 18. CYTOGENETIC STUDY OF SKIN FIBROBLASTS IN A CASE OF ACCIDENTAL ACUTE IRRADIATION.

**Mouthuy M, Dutrillaux B**
**Institut de Progenese, 15 Rue de l'Ecole de Medecine, 75270 Paris Cedex 06, France**
**Mutat Res; 95(1):19-30 1982**

Skin fibroblasts from a heavily irradiated young Algerian who was accidentally exposed to gamma-rays from a 25 Ci iridium-192 source were studied cytogenetically. Biopsies were obtained 25 and 35 mo after irradiation. All types of classical stable chromosomal rearrangements were observed: reciprocal translocations, peri-and para-centric inversions, deletions, shifts, and 3-and 4-break translocations. The numbers of the anomalies and their distribution in the carrier cells are presented. Among the 11 paracentric inversions obtained, one, affecting the chromosome No 13, reproduced a chromosome of an ape, a part probably not occuring by chance, since only 2 paracentric inversions have occurred in the course of the formation of human chromosomes. Only one single clone had clearly developed in vivo. The clone was found in cultures initiated 25 and 35 mo after irradiation. The differences of time and place indicated that it divided and migrated in the organism. Since the frequency of highly abnormal karyotypes was only 0.13, among all abnormal karyotypes, it follows that the more abnormal karyotype, the higher is the probability of clone formation. The percentage of affected cells and the maximal number of breaks detected per cell in the various cultures are presented. Results indicated that information from cytogenetic studies of fibroblasts, even when based on stable chromosomal abnormalities, appear not sufficiently reliable for discriminating between different levels of absorbed dose. (17 Refs)

### 19. UV-REPAIR IS IMPAIRED IN FIBROBLASTS FROM PATIENTS WITH FANCONI'S ANEMIA.

**Schweiger H, Hirsch-Kaufmann M, Schweiger M**
**(c/o M. Schweiger) Abteilung Biochemische Humangenetik, Institut fur Medizinische Biologie und Genetik, Universitat Innsbruck, A-6020 Innsbruck, Austria**
**MGG; 185(3):454-456 1982**

Fanconi's anemia, a hereditary autosomal disease with chromosomal instability, elevated incidence of cancer and clinical symptoms is accompanied by a DNA repair deficiency. Fibroblasts from patients with Fanconi's anemia were found to be impaired in the DNA repair of UV damage. Nucleoid decondensation and recondensation after UV irradiation were less efficient in fibroblasts from patients with Fanconi's anemia than in those from a healthy proband. These data confirm our earlier findings that DNA ligase is deficient in Fanconi's anemia. (Author abstract) (12 Refs)

### 20. ULTRAVIOLET RADIATION SENSITIVITY OF PROLIFERATING AND DIFFERENTIATED HUMAN NEUROBLASTOMA CELLS.

**James M, Mansbridge J**
**(c/o Kidson), Queensland Inst. Medical Res., Bramston Terrace, Herston, Brisbane, 4006, Australia**
**Int J Radiat Biol; 41(5):547-556 1982**

The effects of ultraviolet (UV) radiation were studied on a cloned line of human neuroblastoma cells in proliferative and differentiated growth modes, the latter being induced by serum deprivation. The neuroblastoma cells were found to be unusually sensitive in comparison with HeLa cells when survival was measured by colony formation in soft agar, the differentiated mode being the most sensitive. Ultraviolet radiation sensitivity was associated with very low DNA repair capacity as measured by DNA repair synthesis and by removal of M luteus endonuclease-sensitive sites from irradiated DNA. The greater sensitivity of the differentiated cells appeared to be related to a greater degree of DNA damage at a given UV dose, resulting from altered cell geometry in the growth mode. The neuroblastoma cells showed little or no post-irradiation inhibition of DNA replication at low UV doses, suggesting that it is the repair process rather than the DNA damage which is responsible for inhibiting replication. (Author abstract) (34 Refs)

### 21. RADIATION-INDUCED THYMINE BASE DAMAGE IN REPLICATING CHROMATIN.

**Warters RL, Childers TJ**
**Dept. Radiology, Univ. Utah Medical Center, Salt Lake City, UT, 84132**
**Radiat Res; 90(3):564-574 1982**

When HeLa cells labeled with (3H)thymidine in their parental or mature chromatin DNA or their nascent DNA were exposed to increasing doses of gamma radiation (50-150 kilorad) a greater damage efficiency was observed in nascent chromatin DNA. Elevated thymine damage efficiency in replicating DNA was observed in both irradiated whole cells and isolated nuclei. Both the enzyme digestion (micrococcal nuclease) kinetics of DNA in mature and nascent chromatin, as well as the limit of digestion, were the same in control and irradiated cells. The size of the DNA fragments produced during enzyme digestion and the distribution of the various fragment sizes at equal digestion levels were the same in both control and irradiated cells. The rate at which the excess sensitivity of nascent chromatin DNA decreased to mature chromatin DNA levels was similar to the rate at which nascent chromatin matures, a half-time of slightly more than 2 min in both cases. Hyperthermic exposure reduced the sensitivity of nascent chromatin to parental levels. Deproteinized small fragments of nascent DNA and large fragments of mature or parental DNA were equally sensitive to thymine damage production. When nuclei were exposed to 150 kilorad of gamma radiation and then digested with micrococcal nuclease to a level which solubilizes mainly spacer DNA, the frequency of 5',6'-dihydroxydihydrothymine (tgamma)-type thymine damage in the acid insoluble DNA (principally nucleosome core DNA) was similar to that in whole, undigested chromatin DNA. These results indicate that tgamma-type thymine base damage is uniformly distributed across nucleosome core and spacer DNA. (15 Refs)

### 22. MECHANISM OF CHROMATIN DEGRADATION IN THYMOCYTES OF IRRADIATED RATS. COMMUNICATION 3. POSTRADIATION ACTIVATION OF AUTOLYTIC DNA DEGRADATION IN ISOLATED THYMOCYTE NUCLEI.

**Nikonova LV, Nelipovich PA, Umanskii SR**
**Inst. Biological Physics, Pushchino, USSR**
**Radiobiologiia; 22(2):160-164 1982**

The role of Ca, Mg dependent endonuclease in postradiation DNA degradation was studied in isolated thymocyte nuclei from irradiated (1,000 rads) Wistar rats. Incubation of isolated nuclei in the medium containing Ca++ and Mg++ resulted in marked stimulation of DNA degradation. Incubation of isolated nuclei in the acid medium did not affect the rate of DNA degradation. (9 Refs) (In RUS)

### 23. EFFECT OF IRRADIATION OF HUMAN LYMPHOCYTES DURING G0 AND G1 PHASES ON DNA SYNTHESIS.

**Lychev VA, Poriadkova NA**
**Res. Inst. Medical Radiology, Obninsk, USSR**
**Radiobiologiia; 22(2):243-246 1982**

Human peripheral blood lymphocytes were subjected to gamma irradiation (100, 200, and 400 rads) during the G0 and G1 phases of cell cycle. Irradiation with 100 and 200 rads produced more pronounced inhibition of labeling index in cells irradiated during the end of G1 phase while irradiation with 400 rads was more effective in cells during the G0 phase. These findings indicate that the degree of radiation injury depends upon the time period between irradiation and cell division. (9 Refs) (In RUS)

## OTHER CELLULAR EFFECTS OF IRRADIATION

### 24. IN VITRO RADIOSENSITIVITY OF SIX HUMAN CELL LINES. II. RELATION TO THE RBE OF 50-MEV NEUTRONS.

**Fertil B, Deschavanne PJ, Gueulette J, Possoz A, Wambersie A, Malaise EP**
**Laboratoire de Radiobiologie Cellulaire, Institut Gustave-Roussy, 94805 Villejuif Cedex, France**
**Radiat Res; 90(3):526-537 1982**

The effects of 50million electron volt neutrons on six human cell lines (HF-19, MEWO, SZC, HRT-18, HCT-8, and HT-29) were studied in vitro using the colony forming assay. Cell radiosensitivities were tested with neutron doses up to 5 Gray, resulting in surviving fractions as low as 10(-3) for the most sensitive line, HF-19. The two survival curve models most often used in radiobiology (linear-quadratic and single-hit multitarget) were compared; the models were found to fit the data equally well. (38 Refs)

## THEORETICAL ASPECTS OF RADIATION CARCINOGENESIS

### 25. CHROMOSOMAL REARRANGEMENT AND CARCINOGENESIS.

**Radman M, Jeggo P, Wagner R**
**Departement de Biologie Moleculaire, Universite Libre de Bruxelles, 76 rue des Chevaux, 1640 Rhode-St-Genese, Belgium**
**Mutat Res; 98(3):249-264 1982**

Chromosomal rearrangement (CR) associated with carcinogenesis, CR in human cancer-prone syndromes, carcinogenic CR, induction of CR, role of CR in carcinogenesis, and mechanism of carcinogenesis were examined. To determine whether the ability to induce CR is a general property of carcinogens, 61 carcinogens (45 Ames test-positive, 16 Ames test-negative) were examined. Obtained data supported the hypothesis that the ability to induce CR is correlated with carcinogenesis. The association of CR with human and rodent cancers and with human cancer-prone systems further support the hypothesis. Also suggestive was the finding that DNA from non-malignant cells can transform other non malignant cells, under conditions that may involve CR. Evidence suggesting that some DNA lesions can act as preferential sites for the initiation of DNA exchange is discussed. In addition, the results of several experiments suggested that carcinogens, at least radiation, can act epigenetically to induce recombinant activity. Apparently, carcinogens can act to induce CR by creating or revealing sites of DNA for recombination or by inducing or activating cellular systems resulting in a stimulation of recombination. The ploidy-change class of CR can allow either the amplification of genes, by increasing ploidy, or the expression of recessive genes, by decreasing ploidy. Thus all classes of CR may affect gene expression, and therefore, carcinogenesis. A proposal concerning some of the steps in carcinogenesis, implying that malignancy may be a result of the expression of cellular 'cancer genes' which are either not expressed or insufficiently expressed in normal cells because they are linked with a poorly transcribing control region, is presented. (57 Refs)

### 26. MOLECULAR AND CELLULAR MECHANISMS IN CARCINOGENESIS (MEETING ABSTRACT)

**Rajewsky MF**

**Institut fur Zellbiologie (Tumorforschung), Universitat Essen (GH), Hufelandstrasse 55, D- 4300 Essen 1, W. Germany**

**Molecular and Cellular Mechanisms of Irradiation, March 17-19, 1981, Neuherburg, W. Germany. Gesellschaft fur Strahlen und Umweltforschung MBH 65 pp., 1982.**

Structural modifications of DNA in cellular chromatin are primary events in the multistage process of tumorigenesis initiated by chemical carcinogens, ionizing radiation, and UV light. Among the various classes of chemical carcinogens, the alkylating agents have been particularly well characterized with regard to their reaction products in DNA, and sophisticated methodology (including the use of monoclonal antibodies) has been developed for the detection of specific alkylation products. It is not yet clear which molecular processes are preferentially affected, or set into motion, by carcinogen-modified DNA structures, and which alterations of cellular genetic programmes result in the expression of malignant phenotypes. Among the mechanisms to be considered are different types of mutations, altered patterns of DNN methylation or m-RNA processing, gene rearrangements and amplification, and possibly error-prone DNA repair. There is evidence indicating that in order to become malignantly transformed, cells must be proliferating (or have retained the capacity to re-enter the cell cycle; 'Go-cells') at the time of carcinogen exposure. Furthermore, a number of model systems of carcinogenesis indicate a cell type and differentiation stage-dependency of carcinogenic effect. Certain carcinogen-DNA adducts can be specifically recognized, removed and repaired by cellular enzymes which are expressed to varying degrees in different cell types and tissues, individuals, and species. The differential capacity of cells to repair carcinogen-modified DNA (besides intercellular variations in the metabolic conversion of chemicals to their ultimate reactive derivatives) may constitute one of the determinants for the probability of malignant transformation. (no Refs)

### 27. HOW WELL CAN WE ASSESS GENETIC RISK? NOT VERY.

**Crow JF**

**Univ. Wisconsin, Madison, WI**

**Lauriston S Taylor Lect Radiat Prot Meas; (5):7-31 1981**

The genetic risk associated with environmental radiation is reviewed. Two major uncertainties in genetic risk assessment include the scarcity of human data on induced mutation, and the difficulty of measuring the impact of genetic changes on future generations. The range of mutation-induced effects is very broad. Even in cases where a mutant phenotype is highly specific, it is not possible to identify whether the mutant is the result of radiation or another environmental factor, or a spontaneous occurrence. A mutation rate of zero is to be looked for, and the spontaneous mutation rate should not be accepted as the optimum for the human species. Population kinetics of deleterious mutations, quantitative analyses of mutation rates, and the mutation component of genetic damage are also discussed. (68 Refs)

## ENVIRONMENTAL RADIATION AND PROTECTION STANDARDS

### 28. PROBABILISTIC METHODOLOGY FOR ESTIMATING RADIATION-INDUCED CANCER RISK.

**Dunning DE, Leggett RW, Williams LR**
**Oak Ridge Natl. Lab., Oak Ridge, TN**
**Proceedings of the ANS/ENS Topical Meeting on Probabilistic Risk Assessment, held in Port Chester, New York, September 20, 1981: Available from National Technical Information Service, Springfield, VA, as DE82001474;, 7 pp., 1981.**

The RICRAC computer code was developed at Oak Ridge National Laboratory to provide a versatile and convenient methodology for radiation risk assessment. The code allows as input essentially any dose pattern commonly encountered in risk assessments for either acute or chronic exposures, and it includes consideration of the age structure of the exposure population. Results produced by the analysis include the probability of one or more radiation-induced cancer deaths in a specified population, expected numbers of deaths, and expected years of life lost as a result of premature fatalities. These calculations include consideration of competing risks of death from all other causes. The program also generates a probability frequency distribution of the expected number of cancers in any specified cohort resulting from a given radiation dose. The methods may be applied to any specified population and dose scenario. (Author abstract)

### 29. CRRIS: A COMPUTERIZED RADIOLOGICAL RISK-INVESTIGATION SYSTEM.

**Baes CF, Miller CW**
**Oak Ridge Natl. Lab., Oak Ridge, TN**
**CRRIS: A Computerized Radiological Risk-Investigation System. Available from National Technical Information Service, Springfield, VA, as DE82000136;, 11 pp., 1981.**

The US Environmental Protection Agency (EPA) is responsible for regulating radioactive airborne effluents in the US. A comprehensive, integrated Computerized Radiological Risk Investigation System (CRRIS) is being developed to support EPA's radiation standards development. This modular system consists primarily of five computer codes and their supporting data bases for estimating environmental transport and radiation doses and risks. Health effects are estimated on the basis of a life-table methodology developed by EPA. CRRIS is designed to provide EPA with a reasonable and flexible way of assessing the risk to man associated with radionuclide releases to the atmosphere. (Author abstract)

### 30. RADIATION PROTECTION: THE NCRP GUIDELINES AND SOME CONSIDERATIONS FOR THE FUTURE.

**Sinclair WK**
**National Council on Radiation Protection and Measurements, 7910 Woodmont Ave., Washington, DC, 20014**
**Yale J Biol Med; 54(6):471-484 1981**

The National Council on Radiation Protection and Measurements (NCRP) in the USA and the International Commission on Radiological Protection (ICRP), worldwide, were formed about 1928 and have since made recommendations on appropriate levels of protection from ionizing radiation for workers and for the public. These recommendations and much of the guidance provided by these organizations have usually been adopted by regulatory bodies around the world. In the case of the NCRP, the levels have fallen from 0.1 roentgen per day in 1934 to the current 5 rem per year (a factor of about 5). The present levels recommended by both the ICRP and the NCRP correspond to reasonable levels of risk where the risks of harm from ionizing radiation are compared with the hazards of other, commonly regarded as safe, industries. Some considerations for the future in radiation protection include trends in exposure levels (generally downward for the average exposure to workers) and the improvements in risk estimation; questions of lifetime limits, de minimis levels, and partial body exposures; plus problems of high LET radiations, acceptability of risk, synergisms, and risk systems for protection. (Author abstract) (25 Refs)

## 31. OCCUPATIONAL SAFETY DATA AND CASUALTY RATES FOR THE URANIUM FUEL CYCLE.

**O'Donnell FR, Hoy HC**
**Oak Ridge Natl. Lab., Oak Ridge, TN**
**Occupational Safety Data and Casualty Rates for the Uranium Fuel Cycle. Available from National Technical Information Service, Springfield, VA, as DE82001948:, 88 pp., 1981.**

Occupational casualty (injuries, illnesses, fatalities, and lost workdays) and production data are presented and used to calculate occupational casualty incidence rates for technologies that make up the uranium fuel cycle, including: mining, milling, conversion, and enrichment of uranium, fabrication of reactor fuel; transportation of uranium and fuel elements; generation of electric power; and transmission of electric power. Each technology is treated in a separate chapter. All data sources are referenced. All steps used to calculate normalized occupational casualty incidence rates from the data are presented. Rates given include fatalities, serious cases, and lost workdays per 100 man-years worked, per 10(12) Btu of energy output, and per other appropriate units of output. (Author abstract)

## 32. TRANSURANIUM AND OTHER LONG-LIVED RADIONUCLIDES IN THE TERRESTRIAL ENVIRONS OF NUCLEAR POWER PLANTS. FINAL REPORT.

**Robertson DE, Thomas CW, Perkins RW, Thomas VW**
**Battelle Pacific Northwest Lab., Richland, WA**
**Transuranium and Other Long-lived Radionuclides in the Terrestrial Environs of Nuclear Power Plants. Final Report. Available from National Technical Information Service, Springfield, VA, as DE82003074:, 181 pp., 1981.**

The purpose of this research was to ascertain the contribution of certain radioactive elements, especially transuranics, to the environment from nuclear power plants as opposed to that from fallout due to weapon testing. Of the radioactive nuclides, alpha emitters, eg, plutonium, are considered the most hazardous to human health; hence, the extent to which power plants may release plutonium to the environment is a matter of concern. Samples of soil, plants, and air were taken at four nuclear power plants: Rancho Seco (California), Zion (Illinois), Browns Ferry (Alabama), and Quad-Cities (Illinois). For background purposes, samples were also collected at 10 sites in Idaho, Indiana, Mississippi, Missouri, Montana, North Dakota, Oklahoma, Texas, Washington, and West Virginia that were remote from nuclear plants. Samples were analyzed for plutonium, americium, and curium as well as for a number of other species. Emphasis was on plutonium because the ratio of 238Pu to 239Pu 240Pu can be used to distinguish reactor plutonium from fallout plutonium. The power plant contribution to the environment of the elements tested is negligible. With plutonium, for example, the absolute concentration of the element differed greatly from plant to plant and even from site to site at a given plant; however, the 238Pu, 239Pu ratio was remarkably constant and, with rare exceptions, could not be distinguished from the ratios of background samples. At a few localities, for some elements, a power plant contribution could be recognized. In such cases, despite a power plant contribution, the absolute concentration of the element was below a national background value. (Author abstract)

## 33. MONITORING THE CRITICAL RADIATION EXPOSURE PATHWAYS AT A BWR NUCLEAR POWER STATION.

**Golden JC, Chandrasekaran ES, Kahn B**
**Commonwealth Edison Co., Chicago, IL, 60690**
**Health Phys; 42(6):777-788 1982**

Iodine-131 in milk and gamma radiation from radionuclides in air in the environment of a 3-unit nuclear power station were measured at the levels predicted for airborne effluent. These measurements were part of a modified environmental radiological monitoring program to confirm the population doses computed from radionuclide release rates and environmental transfer models. The limits of detection were lowered relative to conventional monitoring programs by analyzing 21 L samples of milk for 131I and by determining external gamma radiation with a system that combined use of thermoluminescent dosimeters, pressurized ionization chambers, and NaI(Tl) survey meters. For monitoring periods slightly longer than 6 mo, during a time when fallout from atmospheric nuclear tests contributed very little, the av measure, 131I concentration in milk was 0.1 pCi/L for cows on a nearby pasture and 0.02 pCi/L for cows at a more distant control location, compared to predicted values of 0.07 and 0.02 pCi/L, respectively; the av radiation exposure from airborne radionuclides measured at 16 nearby dosimeter locations was 7 mR, compared to the av of predicted values of 4 mR. (Author abstract) (16 Refs)

## 34. NIAGARA FALLS STORAGE SITE, ENVIRONMENTAL MONITORING REPORT FOR 1979 AND 1980.

**Weidner RB, Boback MW**
**Natl. Lead Co. of Ohio, Cincinnati, OH**
**Niagara Falls Storage Site, Environmental Monitoring Report for 1979 and 1980. Available from National Technical Information Service, Springfield, VA, as DE82003005:, 31 pp., 1981.**

The Niagara Falls Storage Site is a 190-acre facility located in Niagara County, New York. It is owned by the US Department of Energy (DOE) and is used for the storage of radioactive residues. This site is managed by NLO, Inc, contract operator of the DOE Feed Materials Production Center near Cincinnati, Ohio. During 1979 and 1980, water and air samples were collected at and near the storage site to provide information about radionuclides in the off-site environment. Results show that uranium and radium concentrations in ground and surface water were within DOE Guide values for uncontrolled areas. Radon-222 in air at the site west boundary exceeded the DOE Guide but off-site monitoring in the general area showed radon-222 concentrations well within the Guide. (Author abstract)

## 35. ENVIRONMENTAL RADIOACTIVITY IN THE FAROES IN 1980.

**Aarkrog A, Lippert J, Dahlgaard H**
**Riso Natl. Lab., DK-4000 Roskilde, Denmark**
**RISO Rep; 448:39pp. 1981**

Measurements of fallout radioactivity in the Faroes in 1980 are presented. Strontium-90 (and 137Cs in most cases) was determined regularly in samples of precipitation, grass, milk, fish, sea water, bread, and drinking water, and in spot check samples of lamb, sea birds, potatoes, sea plants, vegetables, eggs, and human bone. The 90Sr fallout rate in the Faroes in 1980 was approx 0.33 mCi km-2. Based on a diet estimate, the mean content of 137Cs in the Faroes adult was estimated at approx 110 picoCi (g K)(-1). (6 Refs)

### 36. EVALUATION OF THE RADIATION ENVIRONMENT IN THE FOSDALEN MINES.

**Stranden E, Beteig L**
**Statens Inst. for Straalehygiene, Oslo, Norway**
**Evaluation of the Radiation Environment in the Fosdalen Mines. Available from National Technical Information Service, Springfield, VA, as DE81700276, 6 pp., 1981.**

Measurements were made in 1979, 1980 and 1981 in the Fosdalen mines of the concentrations of radon (Rn-222) and thoron (Rn-220) daughters in the atmosphere. These values are given as fractions of the working level (WL). Based on the hours worked by randomly selected miners, the effective dose equivalent has been calculated. In one part of the mines this is up to 60% of the annual dose limit for occupational exposure, in the other parts the doses are probably less than 30% of the annual dose limit. Large short term and seasonal variations occur due to variations in atmospheric pressure and temperature. (Author abstract) (In NOR)

### 37. PROBLEMS OF RADIATION HYGIENE IN CONNECTION WITH THE REPLANTATION OF WASTE BANKS FROM URANIUM MINES.

**Skaucky J, Klener V, Thomas J, Romanidis K**
**Ustav hygieny prace v uranovem prumyslu, Kamenna, Czechoslovakia**
**Cesk Hyg; 27(3):137-144 1982**

The hygienic feasibility of replantation of recent waste and 16th-century waste banks in the region of uranium mines in Czechoslovakia was studied. The use of timber grown on replanted waste banks, the consumption of milk and meat from cattle and sheep grazing in those areas, and of berries from the woods were found not to cause any significant radiation exposure of the population. The erection of permanent dwellings on waste banks is not recommended because of the possibility of significant radiation exposure. (7 Refs) (In CZE)

### 38. EVALUATION OF 133XE RADIATION EXPOSURE DOSIMETRY FOR WORKERS IN NUCLEAR MEDICINE LABORATORIES.

**Piltingsrud HV, Gels GL**
**Nuclear Medicine Lab., Div. Electronic Products, BRH, FDA, Univ. Cincinnati Medical Center, Cincinnati, OH, 45267**
**Health Phys; 42(6):837-848 1982**

Evaluation of past studies of 133Xe dosimetry and nuclear medicine laboratory air concentrations of 133Xe indicates that significant levels of 133Xe may exist in routine operational environments of a nuclear medicine laboratory. This leads to the question of whether present health physics radiation control methods are adequate to keep occupational personnel exposures within acceptable levels. It would appear that if personnel dosimeters (film and TLD badges) respond properly to the radiation of 133Xe, normal health physics control procedures are probably adequate. If they do not respond adequately, personnel exposures may exceed recommended levels and special instrumentation or administrative procedures are called for. Therefore, the first step in studying potential problems in the subject area is to evaluate the response of a variety of personnel radiation dosimeters to 133Xe. This paper describes the methods and materials used to expose personnel dosimeters to known amounts of 133Xe radiations in an exposure chamber constructed at the BRH Nuclear Medicine Laboratory. Also presented are calculated values for Dose Equivalents (DE) in a phantom form external radiation resulting from immersion in clouds having a constant concentration of 133Xe but varying cloud radii. This implies the relative importance of the beta and the X + gamma radiation responses of the personnel dosimeters under various exposure conditions. Results of this study indicate that none of the dosimeter systems evaluated provide adequate performance for use as a primary indicator of the DE resulting from 133Xe radiations for a worker in a nuclear medicine laboratory, and that personnel dosimetry considerations in 133Xe-containing atmospheres are very dependent on the radii of the 133Xe clouds. (Author abstract) (14 Refs)

## REVIEWS AND OTHER STUDIES

### 39. EPIDEMIOLOGICAL STUDIES ON RADIATION CARCINOGENESIS IN HUMAN POPULATIONS FOLLOWING ACUTE EXPOSURE: NUCLEAR EXPLOSIONS AND MEDICAL RADIATION.

**Fabrikant JI**
**Donner Lab., Univ. California, Berkeley, CA, 94720**
**Yale J Biol Med; 54(6):457-469 1981**

The present review provides an understanding of our current knowledge of the carcinogenic effect of low-dose radiation in man, and surveys the epidemiological studies of human populations exposed to nuclear explosions and medical radiation. Discussion centers on the contributions of quantitative epidemiology to present knowledge, the reliability of the dose-incidence data, and those relevant epidemiological studies that provide the most useful information for risk estimation of cancer induction in man. Reference is made to dose-incidence relationships from laboratory animal experiments where they may obtain, for problems and difficulties in extrapolation from data obtained at high doses to low doses, and from animal data to the human situation. The paper describes the methods of application of such epidemiological data for estimation of excess risk of radiation-induced cancer in exposed human populations and discusses the strengths and limitations of epidemiology in guiding radiation protection philosophy and public health policy. (Author abstract) (39 Refs)

### 40. CURRENT CONCEPTS IN ULTRAVIOLET CARCINOGENESIS.

**Granstein RD, Sober AJ**
**(c/o Sober) Dept. Dermatology, Massachusetts General Hosp., Boston, MA, 02114**
**Proc Soc Exp Biol Med; 170(2):115-125 1982**

The pathobiology and epidemiology of UV-induced carcinogenesis are reviewed. The two most common types of nonmelanoma skin cancers in humans and those most related to sun exposure are basal cell carcinoma and squamous cell carcinoma. Nonmelanoma skin cancer in the United States occurs with an incidence of about 400,000 new cases per yr. Phenotypic characteristics associated with the development of this type of cancer include light eye color, fair complexion, and poor tanning ability. While highly pigmented races appear refractory to UV-induced skin carcinogenesis, albinos of such races experience a high incidence of such tumors on sun-exposed areas of the body. Physiologic aging may play a role in the development of nonmelanoma skin cancer. Exposure of human skin to UV radiation results in immediate changes in the nuclear DNA that can be demonstrated with antibodies specific for DNA altered by UV radiation. Modulation of UV-induced skin carcinogenesis by antioxidants, physical factors, carcinogens, retinoids, Beta-carotene, and the immune system are discussed. Malignant melanoma is a neoplasm derived from melanocytes. Both the incidence and death rate from malignant melanoma appear to have been increasing in the past few decades. Although solar exposure appears to be associated with the incidence of melanoma, the relationship is not as clear as for nonmelanoma skin cancer. (128 Refs)

### 41. THE ROLE OF RADIATION AND CHEMICALS IN THE INDUCTION OF MUTATIONS AND EPIGENETIC CHANGES DURING CARCINOGENESIS.

**Trosko JE, Chang CC**
**Dept. Human Development, Coll. Human Medicine, Michigan State Univ., East Lansing, MI, 48824**
**Adv Radiat Biol; 9:2-36 1981**

The relationships between physical and chemical agents and their interactions and the triggering of 'regulatory dysfunction' are reviewed. The abnormal phenotype that is cancer, the multistage nature of carcinogenesis, and the classes of genetic and environmental agents affecting genetic initiation and promotion are discussed. Evidence supporting both the somatic mutation and epigenetic theories of carcinogenesis is reviewed, and an integrative model allowing for mutational and/or epigenetic mechanisms in progression of carcinogenesis is proposed. (255 Refs)

### 42. GENETIC AND SOMATIC RADIATION RISKS: THE EFFECT OF SMALL DOSES.

**Traut H**
**Institut fur Strahlenbiologie, Universitat Munster, Hittorfstrasse 17, D-4400 Munster, W. Germany**
**MMW; 124(17):419-421 1982**

Small doses of radiation such as those received in radiological procedures present the threat of carcinogenesis, teratogenesis, and genetic effects. The risk is, however, so small that the benefits of diagnostic methods outweigh the risk. Radiological diagnostic methods should be used responsibly. Unnecessary repetition of procedures should be avoided. (11 Refs) (In GER)

### 43. RADIATION PROTECTION OPTIMIZATION: PRESENT EXPERIENCE AND METHODS. PROCEEDINGS OF THE EUROPEAN SCIENTIFIC SEMINAR HELD IN LUXEMBOURG, 3-5 OCTOBER, 1979.

**Oudiz A, Uzzan G, Ebert H, Eriskat H**
**Association Euratom-CEA, Departement de Protection, Centre d'Etudes Nucleaires, Boite Postale No 6, 92260 Fontenay-Aux-Roses, France**
**Radiation Protection Optimization: Present Experience and Methods, Proceedings of the European Scientific Seminar held in Luxembourg, 3-5 October, 1979. Oxford, Pergamon Press, 322 pp., 1981.**

Assessment methods of the consequences of populations irradiated and the general point of view of the recommendations of the International Commission of Radiological Protection were determined and their application, regulations of optimization, and justification of irradiation was discussed. Experience in optimization methods is reviewed with respect to a cost-efficiency method used to establish the protection standards for the normal exploitation of the fuel cycle of light-water reactors in the United States and a cost-benefit method for determining the 'as low as reasonably achievable' levels for wastes issuing from light-water reactors. Exploratory studies involving optimization techniques are reviewed, including some decision-making methods, the valuation of detriment, implications of cost benefit analysis for optimization, a general model of optimization of radiation protection and data variability as it applies to pressurized water reactor (PWR) effluent releases, use of optimization methods for radiation protection for nuclear facilities, and use of a multiattribute analysis for the optimization of radioactive release in the PWR fuel cycle. Implementation of optimization methods within the decision making framework and problems encountered are discussed. Comparison of health effects associated with various electric power generation systems in North America and France and public risk perception of various energy systems are reviewed. (140 Refs)

### 44. QUANTIFICATION OF OCCUPATIONAL CANCER.

**Peto R, Schneiderman M**
**Nuffield Dept. Clinical Medicine, Radcliffe Infirmary, Univ. Oxford, Oxford, England**
**Banbury Rep (9): 756 pp., 1981.**

Human exposure to carcinogenic agents was defined and means of preventing such exposure were discussed. Sessions included discussions on asbestos and other mineral fibers (constraints in estimating occupational contributions to current cancer mortality in the United States, proportion of cancer due to exposure to asbestos, cancer among shipyard workers), radiation risks (exposure to ionizing radiation and cancer mortality among workers at the Hanford plant, radon daughters in the induction of lung cancer in underground miners, strategy for the identification of carcinogens in a large chemical company), methodological problems in industry-wide cancer experience (developing protective strategies; mortality studies on lung, pancreas, esophageal, and other cancers in Louisiana; survey of availability of epidemiologic data on humans exposed to animal carcinogens), recent trends in and proportion of occupational cancers in the United States (trends in onset rates, estimating cancer causes), special problems of methodology (holistic approach to monitoring high-risk populations by short-term procedures, industry-sponsored mortality surveillance program), methodology (indicators of exposure trends, epidemiology and occupational classification systems, exposure-based case control approach to discovering occupational carcinogens), broad approaches to occupational cancer quantification (problems in assessing risks from occupational and environmental exposure to carcinogens, differentiating work from life-style in cancer causation), and future needs (record linkage and needed improvements in existing data resources, long-term medical follow-up in Canada). (889 Refs)

### 45. OCCUPATIONAL EXPOSURES TO URANIUM: PROCESSES, HAZARDS, AND REGULATIONS.

**Stoetzel GA, Fisher DR, McCormack WD, Hoenes GR, Marks S**
**Battelle Pacific Northwest Lab., Richland, WA**
**Occupational Exposures to Uranium: Processes, Hazards, and Regulations. Available from National Technical Information Service Springfield, VA, as PNL-3341-USUR-01, 91 pp., 1981.**

The United States Uranium Registry (USUR) was formed in 1978 to investigate potential hazards from occupational exposure to uranium and to assess the need for special health-related studies of uranium workers. This report provides a summary of Registry work done to date. The history of the uranium industry is outlined first, and the current commercial uranium industry (mining, milling, conversion, enrichment, and fuel fabrication) is described. This description includes information on basic processes and areas of greatest potential radiological exposure. In addition, inactive commercial facilities and other uranium operations are discussed. Regulation of the commercial production industry for uranium fuel is reported, including the historic development of regulations and the current regulatory agencies and procedures for each phase of the industry. A review of radiological health practices in the industry - facility monitoring, exposure control, exposure evaluation, and recordkeeping - is presented. A discussion of the nonradiological hazards of the industry is provided, and the final section describes the tissue program developed as part of the Registry. (Author abstract)

## 46. THE CONTRIBUTION OF URANIUM MINERS TO LUNG CANCER HISTOGENESIS.

**Saccomanno G**
**St. Mary's Hosp., Grand Junction, CO**
**Recent Results Cancer Res; 82:43-52 1982**

The development of efforts to regulate health conditions in the uranium mining industry, the evolution of diagnostic technology to evaluate worker health, and the histopathology of lesions which develop in uranium miners are discussed. Methods of collecting sputum for cytology are described. Variables which were found to affect epidemiological analysis included variability in radon daughter levels from mine to mine, in the same mine over periods of time, and even from stope to stope; age of workers and duration of exposure; cigarette smoking in workers; accuracy of records; sample size. Present law provides that the company in which a uranium miner was last employed is liable for compensation to the miner in the event of injury to health. This has sometimes lead to unfair judgements against uranium mining companies. Incidence and cell type of lung cancer occurring in uranium miners, and lung cancer histogenesis (sequential squamous cell metaplasia, benign and premalignant lesions) are reviewed. (7 Refs)

## 47. HYGIENIC STANDARDIZATION OF IONIZING RADIATION.

**Filiushkin IV, Petoian IM**
**USSR Ministry Public Health, Moscow, USSR**
**Gig Sanit; (4):48-51 1982**

Various approaches to the standardization of the levels of ionizing radiation (IR) are discussed with special emphasis on the expected yield of malignant neoplasms after exposure to small doses of IR. Analysis of the cancer morbidity data indicated the absence of the threshold and confirmed the validity of a linear null-hypothesis. (15 Refs) (In RUS)

## 48. ASSESSING THE RISK FOR BREAST CANCER.

**Jankowski NW, McBride CM, Moore A, Shirley RL, Smith F, Jankowski NW, Safford T**
**(c/o The Editor) Patient Care, 16 Thorndal Circle, Darien, CT, 06820**
**Patient Care; 16(5):21-23,30,32-34,43 1982**

Current statistical status of breast cancer, general risk factors related to breast cancer, history of specific irradiation or drug therapy as a risk factor, and the role of benign disease in the development of breast cancer were discussed in a round table meeting. To date, no drug has been shown to increase the risk of breast cancer. Patients with fibroadenosis, sclerosing adenosis, blunt duct adenosis, apocrine metaplasia, plasma cell mastitis, and macrocystic disease have no associated risk of breast cancer. Mammographic reports of 'benign disease' were considered to be reassuring and normal. (6 Refs)

## 49. METABOLIC EPIDEMIOLOGY OF LARGE BOWEL CANCER.

**Hill MJ**
**Central Public Health Lab., Colindale Ave., London NW9, England**
**Gastrointestinal Cancer 1. Decosse JJ and Sherlock P, ed. The Hague, Martinus Nijhoff Publishers, Cancer Treatment and Research, Vol. 3, 452 pp., 1981.**

The epidemiology of large bowel cancer and predisposing and associated diseases are reviewed. Possible causative agents, evidence for the role of bile acids as co-carcinogens, and metabolic epidemiology via results of studies of the histopathology of large bowel cancer and the adenoma-carcinoma sequence are considered. Variables examined in relation to the development of large bowel cancer include geography, sex, socioeconomic group, race, religion, population density, time and cultural environment. Predisposing diseases include adenomatosis coli, cancer family syndrome, and colorectal adenoma. Associated diseases include associated cancers, diseases of fiber depletion, and others. Possible causative agents are stress and physical factors, radiation, immunological factors, virological factors, environmental agents, endogenous agents (cholesterol, bile acids, steroid estrogens, tryptophan metabolites, tyrosine metabolism, and N-nitroso compounds), nutrition, and genetic factors. (154 Refs)

## 50. INTRINSIC RADIOSENSITIVITY OF PROLIFERATING MAMMALIAN CELLS.

**Szumiel I**
**Dept. Radiobiology and Health Protection, Inst. Nuclear Res., 03-195 Warsaw, Poland**
**Adv Radiat Biol; 9:281-321 1981**

Radiation target(s), DNA repair, organization of chromatin, endogenous radiomodifiers, water content and 'structure', cellular recovery from potentially lethal and sublethal damage, and membrane-dependent factors are discussed. Factors determining intrinsic radiosensitivity at the molecular level fall into two categories: factors that alter the quantity of lesions produced in DNA, and factors that are responsible for the interaction of lesions, their accessibility to repair, energy supply, and activity of repair enzymes. (247 Refs)

## 51. RADIATION AND HUMAN HEALTH.

**Gofman JW**
**Univ. California, Berkeley, CA**
**Radiation and Human Health. San Francisco, Sierra Club Books, 908 pp., 1981.**

The relationship between radiation and human health is considered under the following chapter headings: energy interchanges and health, origins of human cancer, induction of cancer and leukemia by ionizing radiation, a systematic approach to the quantitative aspects of radiation carcinogenesis, with personal and public health risk estimates, human epidemiological evidence concerning radiation carcinogenesis, induction of human breast cancer by ionizing radiation, from peak percents to whole-body cancer doses by age at irradiation, practical applications of the whole-body cancer dose, partial-body irradiation and cancer doses for specific kinds of cancers, evidence for a linear or supralinear dose-effect relationship and for the nonexistence of a 'threshold' dose, handling the internal emitter; internal alpha emitter, biologically important, man-made alpha-particle-emitting nuclides (plutonium and other transuranics), lung cancers already produced by plutonium inhalation, plutonium-induced lung cancers in a plutonium energy economy, likely radiation doses and their effects in a nuclear-power economy, ionizing-radiation exposures from natural sources, consumer products, and particular occupations, ionizing-radiation exposures from medical diagnostic and therapeutic irradiation, induction of human leukemia by ionizing radiation, congenital effects of ionizing radiation, and genetic and chromosomal effects of ionizing radiation. (299 Refs)

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# NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

## CHEMICAL CARCINOGENESIS

### 1. TOXICITY OF POLYBROMINATED BIPHENYLS (PBBS) IN DOMESTIC AND LABORATORY ANIMALS

Damstra T, Jurgelski W Posner HS, Vouk VB, Bernheim NJ, Guthrie J Luster M, Falk HL

Natl. Inst. Environmental Health Sciences, Post Office Box 12233, Research Triangle Park, NC, 22709

Environ Health Perspect; 44():175-188 1982

### 2. CHLOROFORM: A REVIEW OF ITS METABOLISM, TERATOGENIC, MUTAGENIC, AND CARCINOGENIC POTENTIAL.

Davidson IW, Sumner DD, Parker JC

c/o Parker ECAO, Environmental Protection Agency, MD-52, Research Triangle Park, MD, 27711

Drug Chem Toxicol; 5(1):1-87 1982

### 3. FORMALDEHYDE IN PRESENT-DAY ENVIRONMENTAL TOXICOLOGY.

Beritic T, Kovac S, Dimov D

Odjel za profesionalne bolesti, Institut za medicinska istrazivanja i medicinu rada, Zagreb, Yugoslavia

Arh Hig Rada Toksikol; 32(4):361-395 1981

In SCR

### 4. HORMONES AS ETIOLOGICAL AGENTS IN NEOPLASIA.

Furth J

Inst. Cancer Res., Columbia Univ. Coll. Physicians and Surgeons, New York, NY

Cancer - A Comprehensive Treatise Vol. 1. Etiology - Chemical and Physical Carcinogenesis. Second Edition. Becker FF, ed. New York, Plenum Press, 714 pp. 1982.

### 5. CURRENT VIEWS ON HORMONES AND BREAST CANCER

Molinatti GM, Limone P

Cattedra di Endocrinologia, Universita di Torino, Corso Polonia, 14, 10126 Turin, Italy

Minerva Med; 73(17):1047-1053 1982

In ITA

### 6. THE CHROMOSOMAL EFFECTS OF THE ORAL CONTRACEPTIVE.

Paisan NP

Tissue Culture and Cytogenetics Unit, Res. Dept., Marie Curie Memorial Foundation, The Chart, Oxted, Surrey, England

J Surg Oncol; 20(2):115-118 1982

### 7. TOXICITY AND CARCINOGENICITY OF NICKEL AND ITS COMPOUNDS. A REVIEW OF THE CURRENT STATUS.

Raithel HJ, Schaller KH

Institut fur Arbeits- und Sozialmedizin, Poliklinik fur Berufskrankheiten, Universitat Erlangen-Nurnberg, Schillerstrasse 25-29, D-8520 Erlangen, W. Germany

Zentralbl Bakteriol Mikrobiol Hyg [B]; 173(1/2):63-91 1981

In GER

### 8. HISTORICAL OVERVIEW OF NITROSOUREA DEVELOPMENT.

Goldin A

Div. Cancer Treatment, NCI NIH, Building 37, Room 5E20 Bethesda, MD, 20205

INSERM Symp; 19:3-11 1981

### 9. PATHOLOGY.

Goyer RA

Natl. Inst. Environmental Health Sciences, Research Triangle Park, NC

JAMA; 247(21):2973-2975 1982

## RADIATION CARCINOGENESIS

### 10. IDENTIFYING THE HEALTH RISKS FROM VERY LOW-DOSE SPARSELY IONIZING RADIATION

Lawyer NA, Friedlander E

Epidemiology Resources, Inc., P.O. Box 57, Chestnut Hill, MA, 02167

Am J Public Health; 72(6):585-588 1982

### 11. RISK OF RADIOLOGICAL EXAMINATIONS.

Jankowski J

Instytut Medycyny Pracy w Lodzi, ul. Olowiana 6, 91-614 Lodz, Poland

Pol Przegl Radiol; 45(6):313-386 1981

In POL

### 12. RADIOBIOLOGY OF RISK ESTIMATES IN MEDICAL IRRADIATION (MEETING ABSTRACT)

Rossi HH

Columbia University, New York, NY

IN: 148th National Meeting of the American Association for the Advancement of Science, January 3-8, 1982, Washington, D.C. American Association for the Advancement of Science 182 pp., 1982.

### 13. RADIATION-INDUCED VASCULAR INJURY AND ITS RELATION TO LATE EFFECTS IN NORMAL TISSUES

Law MP

MRC Cyclotron Unit, Hammersmith Hosp., London W12 OHS, England

Adv Radiat Biol; 9:37-73 1981

### 14. CURRENT CONCEPTS IN ULTRAVIOLET CARCINOGENESIS

Granstein RD, Sober AJ

(c/o Sober) Dept. Dermatology, Massachusetts General Hosp., Boston, MA, 02114

Proc Soc Exp Biol Med; 170(2):115-125 1982

### 15. METABOLIC CHANGES AFTER EXPOSURE TO RADIONUCLIDES.

Kalistratova VS

No affiliation given

Med Radiol (Mosk); 27(4):62-71 1982

In RUS

## DIETARY FACTORS IN CARCINOGENESIS

### 16. CAFFEINE: AN UPDATE.

Oser BL, Ford RA

Bernard L. Oser and Associates, 108-18 Queens Blvd., Forest Hills, NY, 11375

Drug Chem Toxicol; 4(4):311-325 1981

### 17. ANALYSIS OF MUTAGENIC EFFECTS OF FOREIGN SUBSTANCES IN THE FOOD PRODUCTS.

Maganova NB

Inst. Nutrition, Moscow, USSR

Vopr Pitan; (2):3-8 1982

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## EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

### 18. RADIATION EPIDEMIOLOGY (MEETING ABSTRACT)

Marks S

No affiliation given

148th National Meeting of the American Association for the Advancement of Science, January 3-8, 1912, Washington, D.C. American Association for the Advancement of Science 182 pp., 1982.

### 19. EPIDEMIOLOGICAL STUDIES ON RADIATION CARCINOGENESIS IN HUMAN POPULATIONS FOLLOWING ACUTE EXPOSURE: NUCLEAR EXPLOSIONS AND MEDICAL RADIATION.

Fabrikant JI

Donner Lab., Univ. California, Berkeley, CA, 94720

Yale J Biol Med; 54(6):457-469 1981

### 20. EPIDEMIOLOGIC APPROACH TO CANCER.

Guinee VF

Dept. Epidemiology, Univ. Texas System Cancer Center, M.D. Anderson Hosp. and Tumor Inst., Houston, TX

Cancer - A Comprehensive Treatise Vol. 1. Etiology Chemical and Physical Carcinogenesis. Second Edition. Becker FF, ed. New York, Plenum Press, 714 pp., 1982.

### 21. EPIDEMIOLOGY AND EARLY DETECTION OF CANCER OF THE ESOPHAGUS.

Sorouri P

900 Hillside Road, Wilmington, DE, 19807

Gastrointestinal Cancer 1. Decosse JJand Sherlock P, ed. The Hague, Martinus Nijhoff Publishers, Cancer Treatment and Research, Vol. 3, 452 pp., 1981.

### 22. METABOLIC EPIDEMIOLOGY OF LARGE BOWEL CANCER.

Hill MJ

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### 23. EPIDEMIOLOGY OF GASTRIC CANCER AND ITS PRECURSOR LESIONS.

Correa P

Louisiana State Univ. Medical Center, New Orleans, LA, 70112

Gastrointestinal Cancer 1. Decosse JJand Sherlock P, ed. The Hague, Martinus Nijhoff Publishers, Cancer Treatment and Research, Vol. 3, 452 pp., 1981.

### 24. TRENDS IN THE INCIDENCE OF GASTRIC CARCINOMA (MEETING ABSTRACT)

Nobrega FT

Preventive and Internal Medicine, Mayo Clinic, Rochester MN

Eleventh Annual William Beaumont Gastrointestinal Symposium, March 24-26, 1982, El Paso, Texas. William Beaumont Army Medical Center 56 pp., 1982.

### 25. CANCER IN INFLAMMATORY BOWEL DISEASE

Bayless TM, Yardley JH

Johns Hopkins Hosp., Baltimore, MD, 21205

Gastrointestinal Cancer 1. Decosse JJand Sherlock P, ed. The Hague, Martinus Nijhoff Publishers, Cancer Treatment and Research, Vol. 3, 452 pp., 1981.

### 26. GENETIC ASPECTS OF GUT CANCER.

McConnell RB

Broadgreen Hosp., Liverpool, England

Gastrointestinal Cancer 1. Decosse JJand Sherlock P, ed. The Hague, Martinus Nijhoff Publishers, Cancer Treatment and Research, Vol. 3, 452 pp., 1981.

### 27. HOST AND ENVIRONMENTAL FACTORS ENHANCING CARCINOGENESIS IN THE RESPIRATORY TRACT

Nettesheim P, Topping DC, Jamasbi R

Natl. Inst. Environmental Health Sciences, Research Triangle Park, NC, 27709

Annu Rev Pharmacol Toxicol; 21:133-163 1981

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### 28. A SEARCH FOR SAFE DRINKING WATER.

Harsine MA, Schumm HA

Northern Indiana Health Systems Agency, Inc., South Bend, IN

A Search for Safe Drinking Water. Available from National Technical Information Service, Springfield, VA as HRP-0902445/6; 58 pp., 1981.

### 29. OCCUPATIONAL EXPOSURES TO URANIUM: PROCESSES, HAZARDS, AND REGULATIONS

Stoetzel GA, Fisher DR, McCormack WD, Hoenes GR, Marks S

Battelle Pacific Northwest Lab., Richland, WA

Occupational Exposures to Uranium: Processes, Hazards, and Regulations. Available from National Technical Information Service, Springfield, VA, as PNL-3341-USUR-01; 41 pp., 1981.

## CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

### 30. THE ROLE OF RADIATION AND CHEMICALS IN THE INDUCTION OF MUTATIONS AND EPIGENETIC CHANGES DURING CARCINOGENESIS.

Trosko JE, Chang CC

Dept. Human Development, Coll. Human Medicine, Michigan State Univ., East Lansing, MI, 48824

Adv Radiat Biol; 9:2-36 1981

### 31. SOME EFFECTS OF CARCINOGENS ON CELL ORGANELLES.

Svoboda DJ, Reddy J

Dept. Pathology and Oncology, Univ. Kansas Coll. Health Sciences, Kansas City, KS

Cancer - A Comprehensive Treatise Vol. 1. Etiology - Chemical and Physical Carcinogenesis. Second Edition. Becker FF, ed. New York, Plenum Press, 714 pp., 1982.

### 32. CHEMICAL CARCINOGENESIS: INTERACTIONS OF CARCINOGENS WITH NUCLEIC ACIDS.

Rajalakshmi S, Prema M, Sarma D

Dept. Pathology, Univ. Toronto, Toronto, Ontario, Canada

Cancer - A Comprehensive Treatise Vol. 1. Etiology - Chemical and Physical Carcinogenesis. Second Edition. Becker FF, ed. New York, Plenum Press, 714 pp., 1982.

### 33. A MOLECULAR RATIONALE FOR NITROSOUREA INDUCED CYTOTOXICITY.

Tew KD

Lombardi Cancer Center, Div. Medical Oncology, Georgetown Univ., 3800 Reservoir Road, N.W., Washington, DC, 20007

INSERM Symp; 19:61-77 1981

### 34. MODIFICATION OF DNA AND RNA BASES BY THE NITROSOUREAS.

Ludlum DB, Tong WP

Div. Oncology, Dept. Pharmacology and Experimental Therapy, Albany Medical Coll., Albany, NY, 12208

INSERM Symp; 19:21-33 1981

### 35. CALMODULIN AND $CA^{2+}$ IN NORMAL AND TRANSFORMED CELLS.

Veigl ML, Sedwick WD, Vanaman TC

Dept. Microbiology and Immunology, Duke Univ. Medical Center, Durham, NC, 27710

Fed Proc; 41(7):2283-228 1982

### 36. METABOLISM AND TOXICITY OF AFLATOXINS.

Hsieh DP, Wong JJ

Dept. Environmental Toxicology, Univ. California, Davis, Davis, CA, 95616

Adv Exp Med Biol; 136(partB):847-863 1982

### 37. REACTION OF MICROSOMAL AND CYTOSOLIC ENZYMES WITH N-ARYLACETOHYDROXAMIC ACIDS IN THE PRESENCE OF OXYGEN.

Lenk W, Scharmer U

Pharmakologisches Institut, Universitat Munchen, Nussbaumstrasse 26, D-8000 Munchen 2, W. Germany

Adv Exp Med Biol; 136(partB):951-970 1982

### 38. METABOLIC ACTIVATION AND DEACTIVATION MECHANISMS OF DI-, TRI-, AND TETRACHLOROETHYLENES.

Henschler D, Hoos R

Inst. Toxicology, Univ. Wurzburg, Versbacher Strasse 9 Wurzburg D-8700, W. Germany

Adv Exp Med Biol; 136(partA):659-66[illegible] 1982

### 39. METABOLIC ACTIVATION AND HEPATOTOXICITY OF TRICHLOROETHYLENE.

Reynolds ES, Moslen MT

Chemical Pathology Lab., Dept. Pathology, Univ. Texas Medical Branch, Galveston, TX

Adv Exp Med Biol; 136(partA):693-701 1982

### 40. THE ACTIVATING ROLE OF GLUTATHIONE IN THE MUTAGENICITY OF 1,2-DIBROMOETHANE.

van Bladeren PJ, Breimer DD, Rotteveel-Smijs GM, Hoogeterp JJ, Mohn GR, De Groot A, Van Zeeland AA, Van der Gen A

Dept. Pharmacology, Univ. Leiden, P.O. Box 9503, 2300 RA Leiden The Netherlands

Adv Exp Med Biol; 136(partA):809-82[illegible] 1982

### 41. METABOLISM OF POLYCYCLIC AROMATIC HYDROCARBONS IN PLACENTA.

Juchau MR, Chao ST, Namkung MJ

Dep. Pharmacology, Sch. Medicine, SJ-30, Univ. Washington, Seattle, WA, 98195

Adv Exp Med Biol; 136(partA):555-573 1982

## MODIFICATION OF CARCINOGENESIS

### 42. THE INTESTINAL ENZYMATIC BIOTRANSFORMATION SYSTEM: POTENTIAL ROLE IN PROTECTION FROM COLON CANCER.

Hoensch HP, Hartmann F

Medizinische Universitatsklinik, D-7400 Tubingen, W. Germany

Hepatogastroenterology; 28(4):221-228 1981

## VIRAL AND IMMUNOLOGICAL ASPECTS OF CARCINOGENESIS

### 43. THE ONCOGENIC CIRCLE CLOSES.

Rigby PW

Imperial Coll. Science and Technology, London SW7 2BZ, England

Nature; 297(5866):451-453 1982

### 44. ANALYSIS OF CASES OF HEPATIC CELL CARCINOMA THAT TRANSFORMED FROM VIRAL HEPATITIS.

Ichida F, Homma A, Soga K

Third Dept. Internal Medicine, Niigata Univ. Sch. Medicine, Niigata, Japan

Nippon Rinsho; 40(2):468-47[illegible] 198[illegible]

In JPN

### 45. ROLE OF VIRUSES IN THE INDUCTION OF PRIMARY INTRACRANIAL TUMORS.

Walsh JW, Zimmer SG, Perdue ML

Div. Neurosurgery, Univ. Kentucky Medical Center, 800 Rose St., Lexington, KY, 40536

Neurosurgery; 10(5):643-662 1982

## METHODOLOGY IN CARCINOGENESIS RESEARCH

### 46. TRANSLATION OF PHARMACOKINETIC/BIOCHEMICAL DATA INTO RISK ASSESSMENT

Dietz FK, Reitz RH, Watanabe PG, Gehring PJ

Toxicology Res. Lab., Health and Environmental Sciences, Dow Chemical, 1803 Building, Midland, MI, 48640

Adv Exp Med Biol; 136(partB):1399-1424 1982

### 47. IN VITRO ASSAYS FOR THE DIFFERENTIATION OF TUMOR PROMOTORS FROM CARCINOGENS AFTER ROUTINE CARCINOGENESIS BIOASSAYS (MEETING ABSTRACT)

Ward JM, Rice JM

Frederick Cancer Research Center, Frederick, MD

Second Annual Meeting of the Society of Environmental Toxicology and Chemistry, November 22-25, 1981, Arlington, Virgina. Society of Environmental Toxicology and Chemistry 15[illegible] pp., 1982.

### 48. ENVIRONMENTAL CARCINOGENS: SELECTED METHODS OF ANALYSIS. VOLUME 4. SOME AROMATIC AMINES AND AZO DYES IN THE GENERAL AND INDUSTRIAL ENVIRONMENT.

Egan H, Fishbein L, O'Neill IK, Castegnaro M, Bartsch H

Lab. Government Chemist, London, England

IARC Sci Publ (40): 34[illegible] pp., 198[illegible]

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# ICRDB CANCERGRAM

# RADIATION CARCINOGENESIS

SERIES CK06 No. 82/12

DECEMBER, 1982

This Cancergram is a service of the INTERNATIONAL CANCER RESEARCH DATA BANK (ICRDB) PROGRAM of the U.S. National Cancer Institute. Every few weeks, an updated Cancergram containing abstracts of selected cancer-related articles recently published in more than 3000 journals, and dealing with the topic indicated by the above title, is sent to researchers working in this area. These researchers are identified on the basis of the description of their current research project that has been submitted to the ICRDB Program, directly or via granting agencies.

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## RADIATION CARCINOGENESIS IN HUMANS

### 1. MALIGNANCIES AND EXPOSURE OF THE YOUNG TO IONIZING RADIATION.

**Schull WJ, Kato H**
**Center for Demographic and Population Genetics, Univ. Texas Health Science Center at Houston, Houston, TX**
**Cancer Bull; 34(3):84-89 1982**

Risk of radiation-related malignancies in individuals exposed in the first two decades of life in Hiroshima and Nagasaki is described. The relative risk of death due to leukemia in the 'heavily' exposed, particularly among those individuals exposed in the first decade of life, is much higher than the relative risk for exposures at subsequent ages. For the three most common radiation-related malignancies, cancers of breast, lung, and stomach, the absolute risk of death, for age-at-death specific groups, is higher the younger the age at the time of the bombing (ATB). Carcinoma of the thyroid was diagnosed during life more commonly in persons who were less than 20 yr of age ATB. The excess incidence of the malignancy/10(6) person-yr-risk/rad was 2.1, 2.3, 0.33, 0.28, and-0.07 for exposures at less than 10, 10-19, 20-34, 35-49, and 50 or more yr of age ATB, respectively. A study of 339 fatal and nonfatal malignancies

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among young survivors in the period 1950-1974 demonstrated that aside from the increased frequency, the distribution of malignant solid tumors differed little from that seen among individuals who were 20 yr of age or older when exposed. The diminished risk of radiation-related breast cancer among females exposed in the circum-menopausal years suggests that the endocrinologic status and possibly other factors may influence this specific risk. Whether the increased risk extends uniformly to all exposed individuals or whether there are especially vulnerable, 'high-risk' persons, is unknown. (26 Refs)

## 2. PROVIDING FOLLOW-UP IN CHILDHOOD CANCER.

**Napolitano LV, D'Angio GJ, Grossfeld JL, Mauer AM, Miller DR, Sinks LF, Peterson RD**
**(c/o Editor) Patient Care, 16 Thorndal Circle, Darien, CT, 06820**
**Patient Care; 16(13):167-169,173,176-178,180,182,187-188,190-192 1982**

Consequences of therapy in childhood cancer patients are discussed. Findings indicate a drop of 10 or more points in IQ score in children who received 2,400 rad to the brain plus systemic methotrexate. Radiation and cyclophosphamide can cause aspermia, oligospermia, amenorrhea, and, less frequently, the absence of secondary sexual maturation. Exostoses may appear after radiation therapy; these represent derangements of growth rather than benign tumors. Children who have had surgery and who have been treated with bleomycin sulfate may exhibit pulmonary problems upon re-operation. The risk of a second cancer is approx 12% 25 yr posttreatment. Various genetic clusters of diseases appear to be associated with a high incidence of secondary malignant neoplasms. Patients with von Recklinghausen's disease have a tendency to develop neurofibrosarcoma. In follow-up, the former patient is checked monthly at first, then every 6 wk, every 3 mo, and annually by the fifth yr posttreatment. More organized cooperative study follow-ups can help to define and answer some of the questions of long-term side effects of therapy. The presence of alpha-fetoprotein and human chorionic gonadotropin on laboratory assays can be considered as possible signs of germ cell tumors and hepatocellular carcinoma. Cancer 'cure' can only be defined by studying data on large numbers of patients and finding the cut-off point in time after which recurrence of the specific cancer has been highly unusual. Second-line treatment should be administered if no remission occurs and in case of relapse. (5 Refs)

## 3. RADIATION AND RISK FOR THYROID CANCER: ATYPICAL FINDINGS OF A COMMUNITY THYROID RECALL PROGRAM.

**Straub W, Miller M, Sanislow C, Fishbeck W**
**Dept. Radiology, Midland Hosp. Center, Midland, MI, 48640**
**Clin Nucl Med; 7(6):272-276 1982**

Screening of 553 persons for thyroid disease by scan and physical exam was performed. Group I (245) had documented irradiation, with most (85%) receiving 300 R for lymphoid hyperplasia. Group II (308) had only a history of prior irradiation. Abnormal glands were found in 17 of 245 (7%) of Group I with 7 of 245 (3%) having nodular disease. No cancers were found in six of eight (75%) persons with nodular disease having surgery. Abnormal glands were found in 45/308 (14.6%) of Group II with 16/308 (5.2%) having nodular disease. Twelve of 16 (75%) with nodular disease from Group II had surgery and three thyroid cancers were found; in addition, one person from this group had a history of prior surgery for thyroid cancer. The incidence of thyroid cancer in Group I was 0%, Group II was 1.3%, and the combined incidence was 0.7%. The relatively low incidence of thyroid cancer observed is attributed to the relatively late average age at time of irradiation; 22 yr for Group I, 13 yr for Group II (Author abstract) (13 Refs)

## 4. THYROID INJURY AND EFFECTS ON GROWTH AND DEVELOPMENT IN THE MARSHALLESE CHILDREN ACCIDENTALLY EXPOSED TO RADIOACTIVE FALLOUT.

**Sutow WW, Conard RA, Thompson KH**
**(c/o Thompson) Biology Dept., Brookhaven Natl. Lab., Upton, NY**
**Cancer Bull; 34(3):90-96 1982**

Late effects of fallout exposure on Marshallese people, focusing on the effects on the thyroid glands and growth and development of children, are discussed. Until approx 9 yr after exposure the health status of the exposed people did not appear to be significantly different from that of unexposed people. Examinations of newborns of exposed parents did not reveal any detectable abnormalities which might have been related to radiation exposure. The greatest incidence of thyroid nodularity has been noted in the high-dose Rongelap group, particularly in the children exposed at less than 10 yr of age. Among the exposed patients, the ratio of benign lesions to carcinoma appears to be greater in children than in adults. Preventive treatment with thyroid hormone was given to exposed Rongelap people in 1965 and to Ailingnae people in 1969. The pattern of growth and development of the individuals who were children (less than or equal to 18 yr old) on March 1, 1954, regularly followed in the Rongelap people, showed a consistent retardation of stature among boys exposed at less than 10 yr of age; the differences are statistically significant only between ages 9 and 16, apparently because of the administration of thyroid medication after 1963. Stature retardation in exposed girls occurred earlier, was less prominent and of shorter duration than among exposed boys. Osseous maturation among exposed boys was significantly retarded, particularly among boys aged 14-16 yr, compared with that in unexposed age peers. Retardation in osseous maturation among exposed girls occurred primarily among those exposed at less than 5 yr of age and to a very limited degree in those exposed at age 5-10 yr. Adult stature did not differ significantly among exposed and nonexposed individuals. (19 Refs)

## 5. SCINTIGRAPHIC THYROID ABNORMALITIES AFTER RADIATION. A CONTROLLED STUDY WITH 99MTCPERTECHNETATE SCANNING.

**Gonzalez-Villalpando C, Frohman LA, Bekerman C, Favus MJ, Pinsky S, Ryo UY, Shore-Freedman E, Schneider AB**
**(c/o Schneider) Dept. Medicine, Michael Reese Hospital, 2900 South Ellis Ave., Chicago, IL, 60616**
**Ann Intern Med; 97(1):55-58 1982**

We did 99mTcpertechnetate thyroid scintigraphy on 99 subjects with no history of therapeutic irradiation to the head or neck. They were compared with 198 irradiated patients selected from a group of over 1,700 who were evaluated because of radiation treatment for benign head and neck conditions during childhood. The two groups were similar with respect to age and sex distribution. There were significantly more abnormal scintigrams in the irradiated group (55 of 198 patients versus 1 of 99 controls). Even after patients and controls with palpable nodules were excluded from the analysis there were still more abnormal scintigrams in the irradiated group (16 of 150 irradiated versus 1 of 97 control subjects). We conclude that thyroid nodules, including the smaller, nonpalpable nodules discovered by scintigraphy, are related to previous radiation therapy. For persons at substantial risk, such as those who received high-dose treatment (greater than 700 R) during childhood, the data support the use of screening scintigraphy, even with normal findings on palpation. (Author abstract) (13 Refs)

### 6. FAMILIAL RESPIRATORY CARCINOMA: ECOGENETICS OF LUNG CANCER (MEETING ABSTRACT).

**Goffman TE, Hassinger DD, Mulvihill JJ**

**Clinical Epidemiology Branch, National Cancer Institute, Bethesda, MD, 20205**

**Proc Am Soc Clin Oncol; 1:C-573 1982**

Two families with excessive respiratory tract cancers underwent comprehensive evaluation including physical examination, routine laboratory studies, pulmonary function studies, sputum cytologic analysis, assay for quantitative immunoglobulins, tumor markers and lymphocyte karyotyping. In both families, the influences of smoking and, to a lesser extent, occupational exposures were evident risks. Both familes had members with multiple primary cancers and radiogenic tumors in young members, suggestive of inherent predisposition to environmentally induced neoplasia. Further, Family E had a newly recognized syndrome of limb and dental anomalies; and, independently, two members were carriers of a balanced translocation between chromosomes 13 and 14. Effects were made to prevent further respiratory tract cancer deaths, to search for laboratory markers of risk, and to store blood and tissue specimens for assays in development. (no Refs)

### 7. EVIDENCE LINKING ULTRAVIOLET LIGHT AND SKIN CANCER (MEETING ABSTRACT).

**Fitzpatrick TB, Sober AJ**

**Department of Dermatology, Harvard Medical School, Boston, MA**

**148th National Meeting of the American Association for the Advancement of Science, January 3-8, 1982, Washington, D.C. American Association for the Advancement of Science 182 pp., 1982.**

Little argument exists for the linkage of solar exposure and nonmelanoma (basal cell and squamous cell carcinoma) skin cancer (NMSC). Among the evidences cited are: 1) increasing risk with age; 2) increasing risk with increasing hours of solar exposure; 3) increased frequency in those with out-door occupations; 4) increased frequency on sun-exposed areas such as head-neck; 5) increased risk in light skinned Caucasians; 6) rare in Blacks; 7) marked latitude gradient with increased risk in areas of high insolation. Decrease in the atmospheric ozone with increased UVL will surely cause an increase above the current approximately 400,000 cases of NMSC/year in the US. The data linking ultraviolet exposure and malignant melanoma is not so clear-cut except for lentigo malignant melanoma which occurs on sun-damaged, sun-exposed skin of elderly individuals. Evidence cited for the other types of melanoma is as follows: 1) increased Blacks; 3) difference in body distribution in Blacks; 4) difference in distribution patterns in Caucasian men and women with back prominent in both, but lower leg prominent in women and not in men, 5) latitude gradient within countries. The paradoxes in the linkage are the following: 1) outdoor workers are at lower risk than white collar high-in-come professionals; 2) no epidemiologic linkage has been demonstrated between cumulative exposure; 3) areas of greatest exposure on the body surface are not the sites at greatest frequency for melanoma. (no Refs)

## EXPERIMENTAL RADIATION CARCINOGENESIS

### 8. RETINOID INHIBITION OF RADIATION-INDUCED RAT SKIN TUMORS (MEETING ABSTRACT).

**Burns FJ, Sargent EV, McCormick D, Albert RE**
**New York University Institute of Environmental Medicine, New York, NY, 10016**
**Proc Am Assoc Cancer Res; 23:351 1982**

Irradiation of rat skin produces several types of epithelial tumors, including, squamous carcinomas, basal cell carcinomas and a variety of adnexal tumors, each with well-established temporal and dose-response functions. The purpose of the present study was to determine how different exposure schedules to a dietary retinoid affect the yield of tumors induced by ionizing radiation, a direct-acting carcinogen. Male CD-1 rats (Charles River Farms, Wilmington, MA) were irradiated at 28d of age with monoenergetic electrons that penetrated about 1.0 mm into the skin. Retinyl acetate was added to rat lab chow at a concentration of 250 ppm for 20 rats/group as follows: (1) beginning 2 weeks prior to irradiation and ending 1 week after; (2) beginning 1 week after irradiation and continuing indefinitely thereafter; (3) beginning 2 weeks prior to irradiation and continuing indefinitely thereafter. Rats not receiving retinoid began developing tumors about 15 weeks after irradiation and continued to develop tumors reaching about 1.3 tumors/rat at 77 weeks. Neither retinoid treatment schedule 1 or 2 affected the yield of tumors, but schedule 3 reduced the yield of all types of tumors to a level that was indistinguishable from the spontaneous yield in unirradiated non-retinoid treated controls (less than 0.15 tumors/rat). A dietary retinoid when present both during the early and late stages of tumor development produced a powerful inhibitory effect on skin carcinogenesis by ionizing radiation. (no Refs)

### 9. EFFECT OF VITAMIN A AND ANALOGS ON THE INDUCTION OF SQUAMOUS CELL CARCINOMA IN HAIRLESS MICE CAUSED BY SOLAR SIMULATED UV-LIGHT (MEETING ABSTRACT).

**Israili ZH, Razdan R, Willis I**
**Emory University, Atlanta, GA, 30322**
**Proc Am Assoc Cancer Res; 23:806 1982**

The UV component of the sunlight is the primary stimulus for the majority of skin cancers, the most common of human malignancies. Vitamin A and analogs have been shown to prevent certain chemical carcinogen-induced cancers. We tested the effectiveness of vitamin A and analogs as chemopreventive and/or therapeutic agents in a hairless mouse model in which squamous cell carcinoma in the skin is induced by irradiation with solar stimulating UVA (320-400 nm) plus UVB (290-320 nm) in an escalating dose (9.0-15.3 J/cm2, daily, 5 days/wk for 8 wks). Groups of female mice (12-16 wks old) were irradiated and treated as follows: a) N equals 50, controls, b) N equals 46, all-trans-retinoic acid (t-RA, 20 mg/kg body weight), 8 wks during plus 13 wks post-UV, ie, 21 wks, c) N equals 19, t-RA, 13 wks post-UV, d) N equals 10, 13-cis-retinoic acid (c-RA, 80 mg/kg), for 21 wks, e) N equals 10, c-RA, 13 wks post-UV, f) N equals 10, retinol (33 mg/kg), for 21 wks, and g) N equals 10, beta-carotene (33 mg/kg), for 21 wks. Vitamin A and analogs, as suspensions (in 0.3 ml of 1:1 v/v of Carnation milk:water), were given orally 3 times per wk. Mice were maintained on Purina mouse chow and water ad lib, and were observed for 26 wks. No tumors appeared in unirradiated mice given vitamin A analogs. No significant difference was found in the incidence of cancer (papilloma and tumor) at 26 wk in any of the groups of irradiated animals: a) 20/50, b) 16/43, c) 7/16, d) 3/6, e) 4/9, f) 3/8, and g) 5/8. Retinoyl palmitate (300 mg/kg in 0.2 ml corn oil) given orally, 3 times/wk for 6 wks, to 4 mice with large tumors caused some decrease in tumor size. No histological differences were observed in any of the tumors. (no Refs)

### 10. ULTRAVIOLET RADIATION SKIN CARCINOGENESIS (MEETING ABSTRACT).

**Fry RJ, Ley RD, Grube D**
**Oak Ridge National Laboratory, Oak Ridge, TN, 37830**
**Proc Am Assoc Cancer Res; 23:374 1982**

Dose-response relationships of UVR-induced skin cancer have been determined in SKH:hairless-1 mice using an unfiltered Westinghouse FS40 sunlamp (280-400 nm). The suitable doses per fraction were determined from investigation on the induction of pyrimidine dimers, erythema and effects on epidermal cell density. Groups of twelve week-old female mice were treated with one of the following regimens: 1) Thirty-six exposures (3/wk for 12 wk) 0, 250, 500, 1000 J/m2, 2) 0, 250, 500, 1000 or 1500 J/m2 followed by 5 ug 12-O-tetradecanoylphorbol-13-acetate (TPA) 3/wk for 52 wk, 3) 500 J/m2 (3/wk for 24 wk) followed by TPA treatment, and 4) 1500 J/m2 3/wk for 1, 3, 6 or 12 wk followed by TPA treatment. Treatment with TPA alone for one yr did not produce carcinomas but did enhance the expression of UVR-induced tumors. For example, the cumulative incidence at 80 wk after 36 exposures to 1000 J/m(2)/exposure was 15% and 54% when TPA was also given. We have observed a curvilinear dose-response for skin cancer incidence in the absence of TPA treatment and a linear, non-threshold dose-response when TPA was used to maximize the expression of tumors. This suggests that initiation events are induced as a linear, non-threshold function of dose. The incidence of cancer was greater, and the latent period shorter, with 72 fractions than after the same total dose given in fewer fractions. (no Refs)

### 11. TOXIC EFFECT OF ULTRAVIOLET LIGHT ON MELANOCYTES: USE OF ANIMAL MODELS IN PIGMENT RESEARCH.

**Szabo G, Blog FB, Kornhauser A**
**Lab. Electron Microscopy, Harvard Sch. Dental Medicine, 188 Longwood Ave., Boston, MA, 02115**
**JNCI; 69(1):245-250 1982**

Quantitative histologic investigations on the effect of UV radiation on mammalian melanocytes have shown similarities in the response to carcinogenic chemicals, UV radiation, and 8-methoxypsoralen combined with UV radiation. With all three regimens the melanocyte number increased in mice, whereas long-wavelength UV radiation alone did not change the numerical distribution of these cells. Although it is too early to say that similarity in response of these agents indicates identity in harmful effects of these agents, great care should be exercised in the application of psoralens to human skin in a combined treatment with UV radiation. (Author abstract) (22 Refs)

### 12. DEPRESSION OF NATURAL ANTITUMOR RESISTANCE OF C57BL/6 MICE BY LEUKEMOGENIC DOSES OF RADIATION AND RESTORATION OF RESISTANCE BY TRANSFER OF BONE MARROW OR SPLEEN CELLS FROM NORMAL, BUT NOT BEIGE, SYNGENEIC MICE.

**Gorelik E, Herberman RB**
**(c/o Herberman), NCI-Frederick Cancer Res. Facility., Building 560, Room 31-93, Frederick, MD, 21701**
**JNCI; 69(1):89-93 1982**

Small fractionated doses of radiation (4 weekly doses of 179 rad) induced leukemia in 93% of C57BL/6J mice. These leukemogenic doses of radiation were associated with suppression of natural killer (NK) cell activity, as assessed in vitro by cytotoxic activity of spleen cells or in vivo by the ability of irradiated mice to eliminate iv inoculated radiolabeled YAC-1 lymphoma cells. This suppressive effect of irradiation was profound and prolonged, being detectable for at least 7 wk after the last dose of radiation. NK reactivity of irradiated C57BL/6 +/+ or C57BL/6 beige mice could be reconstituted by iv transfer of 10 x 10(6) bone marrow cells or 50 x 10(6) spleen cells from normal C57BL/6 mice. In contrast, transfer of bone marrow or spleen cells from beige donors did not change the NK reactivity of irradiated C57BL/6 +/+ or C57BL/6 bg/bg recipients. It was also shown that the irradiation protocol did not eliminate potentially reactive NK cells, because following interferon incubation (10(3) U/ml), the NK activity of spleen cells of irradiated mice was substantially increased. This study supports the hypothesis of an important role for NK cells in radiation-induced leukemogenesis and forms the basis for exploration of the needed, more direct data on the effects of reconstitution of NK activity on subsequent development of tumors. (Author abstract) (14 Refs)

### 13. STUDIES ON THE LEUKEMOGENIC EFFECTS OF IRRADIATION ON FETAL MICE AT VARIOUS STAGES OF EMBRYONAL DEVELOPMENT.

**Wang J, Zhou J, Wang Z, Wang S, Deng B, Han Y**
**Inst. Nuclear Medicine, Chinese Acad. Medical Sciences, Beijing, People's Republic of China**
**Zhonghua Xueyexue Zazhi; 2(3):141-143 1981**

Pregnant mice were irradiated with 60Co (total dose: 250 R) at the implantation (1-5th day), organogenesis (6-12th day) or fetal (13-18th day) period. The tumor and/or leukemia incidences were 21.9%, 11.5% and 36.5%, respectively, as compared to 4.5% of the unirradiated control. The most common types of leukemia observed were lymphocytic, granulocytic and reticulocytic. The highest mortality rate was also observed in mice irradiated during the fetal period. (14 Refs) (In CHI)

## EXPERIMENTAL RADIATION MUTAGENESIS

### 14. DIFFERENTIAL KILLING AND MUTATION INDUCTION BY ULTRAVIOLET LIGHT OR BENZ(A)PYRENE-4,5-OXIDE BY A UV-RESISTANT CLONE OF CHO-K1 HAVING NORMAL REPAIR ABILITY (MEETING ABSTRACT).

**Newman CN**
**Battelle Pacific Northwest Laboratory, Richland, WA, 99352**
**Proc Am Assoc Cancer Res; 23:194 1982**

An ultraviolet light (UV) resistant line of CHO cells, Mut8-16, was examined and its properties compared to its parent, CHO-K1, following treatment with either UV or the active carcinogen benzo(a)pyrene-4,5-oxide (BP-4,5-0). Survival curves obtained after treatment with UV demonstrated a significantly enlarged shoulder in the mutant compared to CHO-K1 though the slopes of the exponential regions of such curves were identical for the two lines. In spite of the dissimilar survival responses, mutation frequencies (to 6-thioguanine) per UV fluence were indistinguishable. Thus, a differential plot of mutation frequency vs survival indicated an enhanced mutability in the mutant, though at high survival UV fluences only; at lower survival levels such differences were little evident. No significant differences in either excision-repair, replication-repair or postreplication-repair following UV were observed. The mutant and parent showed equal sensitivity to the killing effects of BP-4,5-0 though mutation frequencies in this instance were different. Initial mutation rates at low (less than 6uM) concentrations of carcinogen were lower in the mutant. As the concentration of carcinogen was increased, the mutation frequency responses converged with one another. (no Refs)

### 15. GENOTOXIC EFFECTS OF SUNLIGHT-ACTIVATED WASTE WATER IN CULTURED MAMMALIAN CELLS.

**Strniste GF, Chen DJ, Okinaka RT**
**Genetics Group, Life Sciences Div., Los Alamos Natl. Lab., Los Alamos, NM, 87545**
**JNCI; 69(1):199-203 1982**

Cultured Chinese hamster ovary cells were incubated with dilutions of an oil shale retort process water and exposed to natural sunlight. An enhancement of sevenfold to ninefold was seen in photoinduced cytotoxicity (by a colony-forming assay) and mutagenicity [at the hypoxanthine phosphoribosyltransferase (HPRT) locus] for cells pretreated with the process water compared to effects seen in cells exposed to sunlight only. Significant photoinduced cytotoxicity was also observed in cultured human skin fibroblasts when exposed to the process water before being exposed to near UV (NUV) radiation. The mutation frequencies (determined for the HPRT locus) induced by the process water and NUV radiation were as great as those frequencies seen for far UV light alone. Increases in genotoxicity were observed in excision repair-deficient xeroderma pigmentosum skin fibroblasts when compared to the responses seen in normal cells. Risks to health resulting from the phototransformation of these oil shale retort process waste waters are unassessed at this time. (Author abstract) (19 Refs)

## EFFECTS OF IRRADIATION ON CHROMOSOMES AND DNA

### 16. ROLE OF THE POLYMERASE IN BASE SELECTION FOR IN VITRO DNA SYNTHESIS ON UV-IRRADIATED AND APYRIMIDINIC TEMPLATES (MEETING ABSTRACT).

**Strauss B, Rabkin S, Sagher D, Moore P**
**University of Chicago, Chicago, IL, 60637**
**Proc Am Assoc Cancer Res; 23:47 1982**

In order to understand the role of carcinogen induced lesions in mutagenesis we are studying in vitro DNA synthesis on defined templates containing modifications at particular sites. Phi-chi-174 DNA was UV-irradiated to produce pyrimidine dimers and phage M13 was grown on an ung dut mutant and the DNA treated with uracil N-glycosylase to produce apyrimidinic (AP) sites. DNA synthesis catalyzed by pol I with Mg++ and starting from a restriction fragment primer is blocked one nucleotide before the first pryrimidine of the dimer as previously reported and one base before the putative AP site. Substitution of Mn++ for Mg++ results in extension of the newly synthesized strand, under some conditions, to positions opposite pyrimidine dimers or some AP sites. When single nucleoside triphosphates are used with a UV-irradiated template it is seen that purines are more effective than pyrimidines in extending the chain. With deoxyATP (dATP) at high concentration, dA was inserted opposite the second pyrimdine in the dimer at some sites. It is possible that some dimers were bypassed. Our data indicate that polymerase plays a role in base selection opposite a lesion. Correlations with mutation data in the literature lead us to suggest that in vivo mutational specificity is due to the inherent selectivity of polymerase for nucleotides at a non coding lesion. (no Refs)

### 17. MUTATIONAL SPECIFICITY OF UV LIGHT IN ESCHERICHIA COLI; INDICATIONS FOR A ROLE OF DNA SECONDARY STRUCTURE.

**Todd PA, Glickman BW**
**(c/o Glickman) Lab. Molecular Genetics, Natl. Inst. Environmental Health Sciences, Research Triangle Park, NC, 27709**
**Proc Natl Acad Sci USA; 79(13):4123-4127 1982**

We used the lacI forward mutagenesis system to determine the mutational specificity of UV-induced mutation in a repair-proficient (Uvr+) and a repair-deficient (deltaUvrB) strain of Escherichia coli. The spectra recovered at similar levels of mutagenesis were similar, the exception being a mutational hot spot at site A24 specific to the deltaUvrB strain. Mutations induced at this hotspot, as well as those induced at other mutational hotspots that were found to be common to both the Uvr+ and Uvr- strains, involve G-C to A-T transitions. All of the hotspots are at sites of potential dipyrimidine photoproducts, such as thymine-cytosine and cytosine-cytosine dimers, or of pyrimidine-cytosine photo-product Py-C* lesions. Each of these hotspots occurs at a site in the potential hairpin loop of quasi palindromic sequences. These observations suggest an important role for DNA structure in determining the fate of UV-induced premutational lesions. (Author abstract) (38 Refs)

### 18. ABNORMAL SENSITIVITY TO UV-RADIATION IN CULTURED SKIN FIBROBLASTS FROM PATIENTS WITH HEREDITARY CUTANEOUS MALIGNANT MELANOMA AND DYSPLASTIC NEVUS SYNDROME.

**Smith PJ, Greene MH, Devlin DA, McKeen EA, Paterson MC**
**MRC Clinical Oncology Radiotherapeutic Unit, The Medical School, Hills Road, Cambridge CB2 2OH, England**
**Int J Cancer; 30(1):39-45 1982**

The dysplastic nevus syndrome (DNS) is a preneoplastic melanocyte abnormality which occurs in families affected by hereditary cutaneous malignant melanoma (HCMM). Although environmental exposures, especially solar UV-irradiation, have been implicated as risk factors in sporadic melanoma, the role of such exposures in the pathogenesis of HCMM is unknown. We have studied the in vitro radiation responses of six nontumor skin fibroblast strains from HCMM/DNS patients representing five families. All six HCMM/DNS strains were found to show some degree of enhanced cell killing sensitivity, compared with normal controls, following 254 nm UV-irradiation. The abnormal survival responses appeared to relate to specific characteristics of HCMM/DNS cells since the six strains had essentially normal sensitivity to gamma-radiation. The enhanced photosensitivity was not associated with abnormal patterns in either DNA repair synthesis or UV-induced inhibition and recovery of de novo DNA synthesis. The survival results are consistent with the hypothesis that the genetically determined predisposition to malignant melanoma may directly or indirectly be the consequence of increased susceptibility to UV-induced cellular damage. (Author abstract) (38 Refs)

### 19. THE PRODUCTION OF CHROMOSOME ABERRATIONS IN CHINESE HAMSTER FIBROBLASTS BY GAMMA AND NEUTRON RADIATION.

**Roberts CJ, Holt PD**
**Environmental and Medical Sciences Div., Atomic Energy Res. Establishment, Harwell, Didcot, OX11 ORA, England**
**Int J Radiat Biol; 41(6):645-656 1982**

Chromosomal aberrations were scored in V79/4 Chinese hamster fibroblasts exposed to 60Co gamma-rays and to fast neutrons produced from the 9Be(d,n)(10) B reaction. In order to avoid problems with the variation of aberration induction with the phase of the cell cycle, the cells were irradiated in stationary phase, where they are concentrated in the G1 phase of the cycle. The rbe for the production of dicentrics was 2.7 +-0.2 at a neutron dose of 2.0 Gy; the rbe of the 'one-hit' component of response was 6.4 +-1.1. These rbe values are much lower than those reported for primary human lymphocytes. Graphs of the proportion of cells without a dicentric, centric-ring or acentric fragment, as a function of dose, corresponded closely to the survival curves of the cells, which had been obtained previously, for both radiations. (Author abstract) (26 Refs)

### 20. IDENTIFICATION OF RADIATION-INDUCED THYMINE DERIVATIVES IN CELLULAR DNA (MEETING ABSTRACT).

**Frenkel K, Goldstein MS, Teebor GW**
**Department of Pathology, New York University Medical Center, New York, NY, 10016**
**Proc Am Assoc Cancer Res; 23:261 1982**

We describe a technique for identifying radiation-induced thymine derivatives in cellular DNA. HeLa cells were grown in the presence of 3H-thymidine, irradiated from a 137Cs source (gamma), the DNA isolated and subjected to enzymatic digestion yielding 2'-deoxyribonucleosides. This hydrolysate was analyzed by high pressure liquid chromatography (HPLC) using both 14C-containing and ultra-violet absorbing marker compounds. Modified thymines separated in this manner were subsequently derivatized in the presence of the marker compounds and reanalyzed by HPLC. This analysis led to the unambiguous identification of 5,6-dihydroxy-5,6-dihydrothymidine (thymidine glycol) and 5-hydroxymethyl 2'-deoxyuridine in cellular DNA. The hydrolysate also contained 5,6-dihydroxy-5,6-dihydrothymine (thymine glycol) and 5-hydroxy-5-methyl hydantoin. The presence of these latter compounds was indicative of labilization of the N-glycosyl bond of thymidine glycol and of the rearrangement of the thymine glycol moiety to 5-hydroxy-5-methyl hydantoin. It will now be possible to study the persistance and disappearance of these modified bases in the DNA of irradiated cells and to differentiate spontaneous base loss from enzymatically mediated excision-repair. (no Refs)

### 21. REPAIR OF DNA-PROTEIN CROSSLINKS DURING INHIBITION OF PROTEIN AND DNA SYNTHESIS IN NORMAL HUMAN FIBROBLASTS (MEETING ABSTRACT).

**Taylor WG, Gantt R, Camalier F, Stephens EV**
**National Cancer Institute, Bethesda, MD, 20205**
**Proc Am Assoc Cancer Res; 23:265 1982**

X-rays, ultraviolet light, visible fluorescent light, and various chemicals can induce DNA-protein crosslinks in mammalian cells in culture. Though these lesions are a small proportion of the total damage inflicted on the genome, crosslinks have been implicated in transformation of 3T3 and 10T1/2 cells, induce sister chromatid exchanges, and may be important in carcinogenesis. DNA-protein crosslinks induced by trans-diaminodichloro-platinum (II) were assayed at appropriate times by the membrane alkaline elution procedure of Kohn. Results show that human fibroblasts repair DNA-protein crosslinks while S-phase DNA synthesis is completely inhibited by aphidicolin (10 ug/ml). This clearly shows DNA synthesis is not coupled to the repair of these lesions. When protein synthesis is inhibited with cycloheximide (5 ug/ml), repair of the trans-Pt induced DNA-protein crosslinks is delayed: approx 50% are repaired in 24 hr with little thereafter. Neither the time nor the extent of this partial repair of crosslinks is affected when cells are preincubated for 17 hr with cycloheximide before trans-Pt treatment. These results indicate that the partial repair is not due to turnover in the absence of re-synthesis of required proteins. The repair could result from 'leaky' cycloheximide-insensitive (up to 10 ug/ml) synthesis of a required protein(s) or from the presence of two classes of crosslinks, one of which requires protein synthesis for repair. (3 Refs)

## OTHER CELLULAR EFFECTS OF IRRADIATION

### 22. CHANGES IN THE RELATIVE PROPORTION OF TRANSFORMATION-SENSITIVE POLYPEPTIDES IN GIANT HELA CELLS PRODUCED BY IRRADIATION WITH LETHAL DOSES OF X-RAYS.

**Bellatin J, Bravo R, Celis JE**
**Medical Res. Council Lab. Molecular Biology, Hills Road, Cambridge, England**
**Proc Natl Acad Sci USA; 79(14,part1):4367-4370 1982**

Irradiation of HeLa cells with 1,100 rad (1 rad = 0.01 J/kg = 0.01 Gy) of x-rays yielded a pure population of giant cells 5-7 days after irradiation. These cells do not divide but go through an intermittent DNA synthetic phase. The population of giant cells in S phase (8%) is considerably lower than that of control asynchronous HeLa cells (30%), but 80% of the giant cells go through S phase as determined by 48-hr labeling with [3H]thymidine. Previous studies with high-resolution two-dimensional gel electrophoresis identified 58 [35S]methionine-labeled polypeptides common to human epithelial amnion cells and lung fibroblasts, whose rate of synthesis is sensitive to neoplastic transformation. These polypeptides also have been identified in HeLa cells and other transformed human cells such as Detroit 98, Chang liver, F1-amnion, and WISH-amnion. After irradiation of HeLa cells and giant cell formation, the relative proportions of most of the transformation-sensitive polypeptides (43 of 47) reverted to levels similar to those observed in non-tumorigenic cells. This suggests that their relative proportions are dependent on the growth properties of the cells. In particular, the relative proportions of three polypeptides (designated 12g and 60d1 in isoelectric focusing and 27b in nonequilibrium pH gradient electrophoresis) were not affected, indicating that their reduced amounts in transformed cells could reflect a fundamental change that develops during transformation. (Author abstract) (17 Refs)

### 23. BIOLOGICAL EFFECTS OF RADIATION WITH HEAVY IONS.

**Kiefer J**
**Strahlenzentrum der Universitat, D-6300 Giessen, W. Germany**
**Naturwissenschaften; 69(6):260-265 1982**

Experiments with accelerated heavy ions may contribute to the understanding of biological radiation action. After outlining the theoretical background experiments are described which were carried out at the UNILAC-machine (Gesellschaft fur Schwerionenforschung, Darmstadt, Germany) where ions up to uranium can be accelerated to maximal specific energies of 10 MeV/u. Yeast cells served as biological test systems with the synthesis of ribosomal RNA (r-RNA), colony-forming ability and mutation induction as experimental endpoints. A relationship between action and energy deposition by individual particles can be demonstrated for the inhibition of r-RNA synthesis, in other cases the ion energy plays also an important role indicating that the interaction of delta-electrons from different particles contributes significantly to the biological effect. (Author abstract) (13 Refs) (In GER)

### 24. EFFECT OF AGE ON SENSITIVITY OF HUMAN LYMPHOCYTES TO RADIATION. A BRIEF NOTE.

**Kutlaca R, Seshadri R, Morley AA**
**Dept. Hematology, Flinders Univ. South Australia, Bedford Park, South Australia 5042, Australia**
**Mech Ageing Dev; 19(2):97-101 1982**

Survival of human lymphocytes after x-ray and ultraviolet irradiation was studied in individuals of various ages using a technique of cloning in soft agar. There was no effect of age on survival after ultraviolet irradiation but lymphocytes from elderly individuals were approx twice as sensitive to x-radiation as lymphocytes from young individuals. The results are relevant to the possible importance of DNA damage and repair in cellular ageing. (Author abstract) (13 Refs)

## ENVIRONMENTAL RADIATION AND PROTECTION STANDARDS

### 25. SOME CONFOUNDING FACTORS IN THE STUDY OF MORTALITY AND OCCUPATIONAL EXPOSURES.

**Gilbert ES**
**Pacific Northwest Lab., P.O. Box 999, Richland, WA, 99352**
**Am J Epidemiol; 116(1):177-188 1982**

With the recent interest in the study of occupational exposures, the impact of certain selective biases in the groups studied is a matter of some concern. In this paper, data from the Hanford nuclear facility population (southeastern Washington State, 1947-1976), which includes many radiation workers, are used to illustrate a method for examining the effect on mortality of such potentially confounding variables as calendar yr, length of time since entering the industry, employment status, length of employment, job category, and initial employment yr. The analysis, which is based on the Mantel-Haenszel procedure as adapted for a prospective study, differs from most previous studies of occupational variables which have relied primarily on comparing standardized mortality ratios (utilizing an external control) for various subgroups of the population. Results of this analysis confirm other studies in that reduced death rates are observed for early yr of follow-up and for those with higher socioeconomic status (as indicated by job category). In addition, workers employed less than 2 yr and especially terminated workers are found to have elevated death rates as compared with the remainder of the study population. It is important that such correlations be taken into account in planning and interpreting analyses of the effects of occupational exposure. (Author abstract) (21 Refs)

### 26. EPIDEMIOLOGICAL STUDIES OF RADIATION WORKERS: PRELIMINARY COMMUNICATION.

**Schofield GB**
**British Nuclear Fuels Ltd., Sellafield, Seascale, Cumbria CA20 1PG, England**
**J R Soc Med; 75(6):450-456 1982**

British Nuclear Fuels Limited has embarked on a study of the mortality data among those of its workforce who were employed prior to 1 January 1976. The study covers a total population of about 41,000 current and ex-employees, but is initially concerned with a radiation worker cohort of 7,500 at the Sellafield establishment where the highest radiation doses are received. Tracing of the health status of ex-employees has been undertaken using the services provided by the Office of Population Censuses and Surveys (OPCS) and the Department of Health and Social Security (DHSS) and it is expected that ultimately the level of trace will be better than 97%. Mortality data not specifically related to radiation workers are included and relate to male deaths among serving staff and pensioners during the years 1962-1972. Those observed deaths (O) are compared on an age standardized basis with those expected (E) from the general population, the ratio O/E being about 1 for all cancers and less than 1 for non-cancer deaths. This pattern is consistent with the well known 'healthy worker' effect seen in industry. (Author abstract) (4 Refs)

### 27. INDUSTRIAL HYGIENE REPORT. HOMESTAKE MINING COMPANY, LEAD, SOUTH DAKOTA.

**Zumwalde RD, Ludwig HR, Dement JM**

**Nat'l. Inst. Occupational Safety and Health, Cincinnati, OH**

**Industrial Hygiene Report, Homestake Mining Company, Lead, South Dakota. Available from National Technical Information Service, Springfield, VA, as PB82-179961, 267 pp., 1982.**

Worker exposures to free silica (7631869), radon (10043922) daughters, arsenic (7440382), and asbestos (1332214) fibers were determined at the Homestake Mining Company (SIC-1041) in Lead, South Dakota from July 12 to 23, 1977. The mining operation was being investigated due to an elevated incidence of deaths from malignant and nonmalignant respiratory diseases in the mining population. About 968 employees worked in the underground operations on 35 levels from 1,700 to 8,000 feet. Approx 170 employees representing 90% of the job titles were sampled for an entire work shift using personal filters. Data for free silica was used from a survey conducted in 1976 for the mine. Midget impinger samples were collected for dust. Samples were collected from 448 miners during an entire work shift with each crew over a 2 wk period. Work practices were documented. The authors conclude that mean exposures for free silica, radon daughters, arsenic, and asbestos fibers are within OSHA standards for most job classifications. They suggest that the potentiating effect of the contaminants could predispose some workers to respiratory diseases. They recommend a continuing education program for job hazards, maintenance procedures, and cleanup methods, and to ensure that they understand how to use respiratory protective equipment and protective clothing. They suggest sealants to contain radioactive contamination from rock, and reduction of dust concentrations. (Author abstract)

### 28. CHARACTERIZATION OF PLUTONIUM IN GROUND WATER NEAR THE IDAHO CHEMICAL PROCESSING PLANT.

**Cleveland JM, Rees TF**

**United States Geological Survey, MS 412, Lakewood, CO, 80225**

**Environ Sci Technol; 16(7):437-439 1982**

Ground water near the disposal well at the Idaho Chemical Processing Plant contained very low concentrations of plutonium, while water at greater distances did not contain detectable Pu. Levels of Pu were low because of the absence of organic complexing agents to stabilize it against precipitation or sorption. Pu was detectable in one well as an uncomplexed tetravalent ion. The ability of strong complexes to solubilize Pu is demonstrated. The need for isolating Pu-containing wastes from dissolved organic species in ground water is emphasized. (6 Refs)

### 29. IONIZING RADIATION.

**Voelz GL**
**Health Div., Los Alamos Scientific Lab., Los Alamos, NM**
**Occup Health Saf; 51(7):34-37 1982**

The clinical evaluation of occupationally related exposure to ionizing radiation is considered. Observed health effects due to radiation have occurred mostly after acute exposures. Low dose effects are not easily observable. In 1975 the percentage of total collective radiation doses to workers (185,000 man rem) was distributed as follows: medical workers 29%; industrial users of radionuclides 20%; workers in the nuclear fuel cycle 14%; dental workers 10%; research and development workers 6%; and others 11%. The av dose for workers monitored for radiation in the United States was 0.13 rem/yr. Natural background radiation and medical use of radiation are responsible for 94% of the total exposure to the general population. Causation is not provided by epidemiologic association alone, and failure to recognize this has led to confusion concerning risk assessment. Present knowledge suggests that cancer risk after radiation is the most critical component of the various associated risks, including genetic and prenatal teratogenic effects. Thus cancer risks must be considered a key factor in developing radiation exposure standards. (11 Refs)

### 30. RISKS OF SMALL RADIATION DOSES.

**Fritz-Niggli H**
**Strahlenbiologisches Institut, August Forel-Strasse 7, CH-8029 Zurich, Switzerland**
**Praxis; 71(20):871-880 1982**

Human exposure to man-made radiation is due primarily to diagnostic and therapeutic uses of radiation in medicine. The mean bone marrow dose/yr for the Swiss population is 12 millirem from artificial sources, compared with 120 millirem for normal background radiation. Artificial radiation may increase lifetime cancer risk by 0.05%/rem. The somatic and genetic risks may be significantly increased for patients and medical personnel. (9 Refs) (In GER)

## REVIEWS AND OTHER STUDIES

### 31. PROBLEMS IN ASSESSING THE CANCER RISKS OF LOW-LEVEL IONIZING RADIATION EXPOSURE. VOLUME 1.

**Comptroller General of the United States**
**(c/o Superintendent of Documents), United States General Accounting Office, Document Handling and Information Services Facility, P.O. Box 6015, Gaithersburg, MD, 20760**
**Problems in Assessing the Cancer Risks of Low-Level Ionizing Radiation Exposure. Volume 1. Washington, D. C., U. S. General Accounting Office, 35 pp., 1981.**

The scientific issues involved in determining the cancer risks of low level radiation exposure are analyzed and the current status of knowledge of these risks are assessed. Key findings, conclusions, and recommendations in the complete Technical Report, Volume 2, are discussed in a nontechnical manner. Basic objectives of the study were to determine conclusions, if any, on low-level effects of ionizing radiation, and about the best direction for current and future research. A literature search was conducted to identify articles of interest, and researchers were interviewed. Issues are introduced and a brief primer on radiation facts and concepts is presented. The fundamental aspects of exposure to ionizing radiation to subcellular and cellular organisms are reviewed, including chemical effects of ionizing radiation, DNA damage and repair, the immune system, and experiments with cultured mammalian cells. Problems of epidemiological analyses, tests of dose-response curves, cancer incidence in Hanford workers, a survey of multiple myeloma patients, childhood leukemia mortality in Utah, estimation of latency, and susceptible groups in the population are discussed. The Federal radiation research program is reviewed with respect to funding, types of radiation research, epidemiology, animal research, research on mechanisms of radiation carcinogenesis, and current efforts to improve the Federal radiation research program. Conclusions and recommendations on the Federal radiation research program are made. (no Refs)

## 32. PROBLEMS IN ASSESSING THE CANCER RISKS OF LOW-LEVEL IONIZING RADIATION EXPOSURE VOLUME 2.

**Comptroller General of the United States**

**(c/o Superintendent of Documents), United States General Accounting Office, Document Handling and Information Services, P.O. Box 6015, Gaithersburg, MD, 20766**

**Problems in Assessing the Cancer Risks of Low-Level Ionizing Radiation Exposure. Volume 2. Washington, D. C., U. S. General Accounting Office, 690 pp., 1981**

The scientific effects of low-level ionizing radiation exposure were studied in order to draw definite conclusions and to determine the best direction for current and future research. Radiation facts and concepts helpful in understanding the technical chapters are reviewed and a history of radiation protection standards is presented. The fundamental biological aspects of exposure to ionizing radiation are reviewed, including chemical effects, cell inactivation, cell mutation, cell transformation, radiation damage and repair, damage and repair of the immune system, and a two-target model of cell transformation. The current status of research of radiation effects on laboratory-grown cells is summarized, describing radiation experiments in which cells are killed, mutated or transformed. Statistical analyses of studies of groups of persons exposed to radiation are presented, and include discussion of the dose-response relationship, latency period, susceptibility, radiation-sensitive population subgroups, the Hanford workers survey, a General Accounting Office analysis of the Hanford data, an unblinded survey of multiple myeloma, and childhood leukemia mortality in Utah. Federal research on the biological effects of ionizing radiation is reviewed, including a report by the National Institute for Occupational Safety and Health, and research programs funded by Federal agencies. (517 Refs)

## 33. MODIFICATION OF PHOTOCARCINOGENESIS BY CHEMICAL AGENTS.

**Urbach F, Forbes PD, Davies RE**

**Center Photobiology, Skin and Cancer Hosp., Temple Univ. Sch. Medicine, Philadelphia, PA, 19140**

**JNCI; 69(1):229-235 1982**

The evidence is long standing and compelling that chemical agents can modify the carcinogenic effects of light. Various types of chemical-light interaction are discussed and events in chemical photocarcinogenesis, chemically enhanced photocarcinogenesis, and promotion of photocarcinogenesis are described. Specific examples of each type of process are given, and the importance of interaction of various wavelengths of UV radiation for these processes is stressed. (Author abstract) (15 Refs)

## 34. RISKS OF NUCLEAR ENERGY AND LOW-LEVEL IONIZING RADIATION. REPORT OF AN AMA ADVISORY PANEL TO THE COUNCIL ON SCIENTIFIC AFFAIRS OF THE AMERICAN MEDICAL ASSOCIATION.

**Ashare AB, Lave LB, Lincoln TA, Lushbaugh CC, Murray SS, Saenger EL, Schaefer WW, Tapper CJ, Wald N**

**Dept. Nuclear Medicine, St. Elizabeth's Hosp., Boston, MA**

**Risks of Nuclear Energy and Low-Level Ionizing Radiation. Report of an AMA Advisory Panel to the Council on Scientific Affairs of the American Medical Association Monroe, WI, American Medical Association, 40 pp., 1981**

Health effects of some of the sources of electricity that can be used at present and in the future are reported focusing on the health effects of nuclear energy. Various documents including the 1979 report of the National Academy of Sciences, 'Risks Associated with Nuclear Power', and the 'Report of the President's Commission on the Accident at Three Mile Island' are reviewed. Aspects related to the peaceful uses of nuclear energy are considered. Because some of the reviewed documents are comprehensive compilations of scientific knowledge about the adverse health effects of radiation, the literature is not summarized in detail. The main health-related issues are defined in an attempt to prepare a report understandable to nonradiologist physicians and which would also take note of people's major questions and concerns. Generating electricity with nuclear energy, mine tailings and nuclear wastes, occupational radiation exposure, health effects of ionizing radiation, risks of ongoing nuclear operations, public perception of risk, and modifications of the 1978 American Medical Association report are discussed. Relevant definitions and abbreviations are presented. One of the recommendations is that a continuing emphasis should be placed on research that is capable of determining more precisely the health effects of low-level ionizing radiation. (69 Refs)

## 35. BREAST CANCER EPIDEMIOLOGY AT PRESENT.

**Morales S A**

**Epidemiolgo del Servicio de Salud Norte y del Ministerio de Salud, Chile**

**Rol Hosp San Juan Dios 29(1):16-23 1982**

Data from the early 1900's to the present on various epidemiological factors relating to breast cancer are studied. Menarche at an early age is considered a protective factor and prolonged use of estrogens a risk factor. Women who are multiparous and experience their first term pregnancy before the age of 24 yr are less likely to develop breast cancer. The role of breast-feeding as a protective factor was found to be secondary to the significance of the age at first pregnancy. There is a protective factor in early menopause. A small proportion of breast cancers found within families has been related to an autosomal dominant gene on Chromosome 10. Diets high in saturated fats and body surface measurements are risk factors. Socioeconomic factors, use of hair dyes, and exposure to ionizing radiation were also considered. The highest occurrence rate was found in the United States, Canada, and Northeastern Europe. In Chile, the mortality rate of breast cancer as compared to all other cancer mortalities is 5%. The highest occurrence rate is in the cities. (15 Refs) (In SPA)

### 36. PRINCIPLES IN RADIATION MEDICINE HAZARDS.

**Ilbery PL**
**Commonwealth Dept. Health, Sydney, Australia**
**Australas Radiol; 25(3):312-319 1981**

Minimizing radiation medicine hazards are discussed with respect to radiobiology and the harm/benefit, radiation medicine practice, and licensing. Regulation of medical use of radiation is necessary in order to protect the health and safety of users and patients alike. Medical radiation exposure of a patient differs from exposure from other sources in that the risk incurred is to a person who is in receipt of direct benefit by virtue of improved diagnosis or therapy. Radiomimetics, radioisotopes, and radiodiagnostics are discussed. (3[illegible] Refs)

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## CHEMICAL CARCINOGENESIS

### 1. ASBESTOS CARCINOGENESIS: ASBESTOS INTERACTIONS AND EPITHELIAL LESIONS IN CULTURED HUMAN TRACHEOBRONCHIAL TISSUES AND CELLS.

Haugen A, Harris C
Div. Cancer Cause and Prevention, NCI, Bethesda, MD
Recent Results Cancer Res; 82:32-4[illegible] 1982

### 2. REVIEW: ORAL CONTRACEPTIVES AND MENOPAUSAL ESTROGENS IN RELATION TO BREAST NEOPLASIA.

Brzezinski A, Schenker JG
Dept. Obstetrics and Gynecology, Hadassah Univ. Hosp., POB 12000, 91120 Jerusalem, Israel
Isr J Med Sci; 18(4):433-438 1982

### 3. LIVER DISEASES DUE TO HORMONAL CONTRACEPTIVES.

Lie TS
Chirurgische Klinik und Poliklinik, Universitat, Sigmund-Freud-Str. 25, D-5300 Bonn 1, W. Germany
MMW; 124(20):489-494 1982
In GER

## RADIATION CARCINOGENESIS

### 4. THE WORK OF THE NRPB 1977/80 AND A REVIEW OF THE FIRST 10 YEARS.

National Radiological Protection Board
Natl. Radiological Protection Board, Chilton, Didcot, Oxfordshire OX11 0RQ, England
The Work of the NRPB 1977/80 and a Review of the First 10 Years. Chilton, Didcot, Oxfordshire, National Radiological Protection Board, 70 pp., 1981.

## DIETARY FACTORS IN CARCINOGENESIS

### 5. ALCOHOL AND CARCINOGENESIS.

Seitz HK, Czygan P, Kommerell B
Schwerpunkt Gastroenterologie, Medizinische Universitatsklinik, Bergheimer Str. 58, D-6900 Heidelberg 1, W. Germany
Leber Magen Darm; 2(3):9[illegible]-107 1982
In GER

### 6. ZINC, COPPER, AND MANGANESE IN IMMUNE FUNCTION AND EXPERIMENTAL ONCOGENESIS.

Beach RS, Gershwin ME, Hurley LS
Dept. Internal Medicine, Div. Rheumatology-Clinical Immunology, Univ. Calif., Davis, CA, 95616
Nutr Cancer; 3(3):172-191 1982

## EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

### 7. TRENDS IN CANCER INCIDENCE: CAUSES AND PRACTICAL IMPLICATIONS. PROCEEDINGS OF A SYMPOSIUM HELD OSLO, NORWAY, 6-7 AUGUST 1980.

Magnus K
The Cancer Registry Norway, Montebello, Oslo 3, Norway
Trends in Cancer Incidence: Causes and Practical Implications. Proceedings of a Symposium held Oslo, Norway, 6-7 August 1980. Washington, D.C., Hemisphere Publishing Corporation, [illegible] pp., 1982.

## ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN CARCINOGENESIS

### 8. QUANTIFICATION OF OCCUPATIONAL CANCER.

Peto R, Schneiderman M
Nuffield Dept. Clinical Medicine, Radcliffe Infirmary, Univ. Oxford, Oxford, England
Banbury Rep (9): [illegible]56 pp., 1981.

### 9. NASAL CARCINOMA IN WOODWORKERS: A REVIEW.

[illegible] JH
Sch. Medicine, Uniformed Services Univ. Health Sciences, 4301 Jones Bridge Road, Bethesda, MD, 20814
JOM; 24(7):526-530 1982

### 10. AIR POLLUTION AND CANCER. A REVIEW OF EXPERIMENTAL INVESTIGATIONS.

Madsen ES, Nielsen PA, Pedersen JC
(c/o Nielsen), Stigardsvej 2, DK-2900 Hellerup, Denmark
Ugeskr Laeger; 144(23):1719-1721 1982
In DAN

### 11. AIR POLLUTION AS A RISK FACTOR IN LUNG CANCER.

Vena JE
Dept. Social and Preventive Medicine, State Univ. New York at Buffalo, 2211 Main St., Buffalo, NY, 14214
Am J Epidemiol; 116(1):42-56 1982

### 12. INHALATION CARCINOGENESIS: AN OVERVIEW.

Chretien J
Hopital Laennec, 42 rue du Sevres, F-75007 Paris, France
Recent Results Cancer Res; 82:1-10 1982

### 13. THE NITROSAMINE HAZARD.

Yonkers AJ
Dept. Otolaryngology, Univ. Nebraska, Omaha, NE
Ear Nose Throat J; 61(7):407-414 1982

## CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

### 14. ONCOGENES OF SPONTANEOUS AND CHEMICALLY INDUCED TUMORS.

Weinberg RA
Center for Cancer Res., Massachusetts Inst. Technology, Cambridge, MA, 02139
Adv Cancer Res; 36:14[illegible]-163 1982

### 15. RELATIONSHIP OF DNA TERTIARY AND QUATERNARY STRUCTURE TO CARCINOGENIC PROCESSES.

Lipetz PD, Galsky AG, Stephens RE
Dept. Radiology, Ohio State Univ., Columbus, OH, 43210
Adv Cancer Res; 36:16[illegible]-210 1982

### 16. ROLE OF ENZYMATIC METHYLATION OF DNA IN CELL DIFFERENTIATION AND TRANSFORMATION.

Fedorov NA
Central Res. Inst. Hematology and Blood Transfusion, Moscow, USSR
Eksp Onkol; 4(1):3-11 1982
In RUS

### 17. HYDROGEN ION DYNAMICS AND CANCER: AN APPRAISAL.

Harguindey S
Dept. Thoracic Surgery and Oncology, Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
Med Pediatr Oncol; 10(3):217-236 1982

## MODIFICATION OF CARCINOGENESIS

### 18. CARCINOGENESIS AND BIOLOGICAL EFFECTS OF TUMOR PROMOTERS.

Hecker E
Ins. Biochemistry, German Cancer Res. Center, Heidelberg, W. Germany
Carcinogenesis 7: 664 pp., 1982.

## VIRAL AND IMMUNOLOGICAL ASPECTS OF CARCINOGENESIS

### 19. AVIAN LEUKEMIA VIRUSES: ONCOGENESES AND GENOME STRUCTURE.

Graf T, Stehelin D
Inst. Virology, German Cancer Res. Center, In Neuenheimer Feld 280, 6900 Heidelberg, W. Germany
Biochim Biophys Acta; 651(4):245-27[illegible] 1982

### 20. HYPERPLASTIC AND NEOPLASTIC ERYTHROPROLIFERATIVE DISEASES INDUCED BY ONCOGENIC MURINE RETROVIRUSES.

Scolnick EM
Lab. Tumor Virus Genetics, NCI, Bethesda, MD, 20205
Biochim Biophys Acta; 651(4):273-283 1982

## METHODOLOGY IN CARCINOGENESIS RESEARCH

### 21. MOLECULAR EPIDEMIOLOGY AND CARCINOGEN-DNA ADDUCT DETECTION: NEW APPROACHES TO STUDIES OF HUMAN CANCER CAUSATION.

Perera FP, Weinstein IB
Div. Environmental Sciences, Columbia Univ., New York, NY 10032
J Chronic Dis; 35(7):581-600 1982

### 22. AN EVALUATION OF ASSAY PROCEDURES FOR DETECTION OF TUMOR PROMOTORS.

Sivak A
(c/o P. H. Lohman) Medical Biological Lab. TNO, P.O. Box 45, 2280 AA Rijswijk, The Netherlands
Mutat Res; [illegible]:377-387 1982

### 23. DNA REPAIR ASSAYS AS TESTS FOR ENVIRONMENTAL MUTAGENS. A REPORT OF THE U.S. EPA GENE-TOX PROGRAM.

Larsen KH, Brash D, Cleaver JE, Hart RW, Maher VM, Painter RB, Sega GA
Environmental Mutagen Information Center, Oak Ridge Natl. Lab., Oak Ridge, TN, 37830
Mutat Res; 98(3):28[illegible]-318 1982

### 24. AN EVALUATION OF THE HOST-MEDIATED ASSAY AND BODY FLUID ANALYSIS. A REPORT OF THE U.S. ENVIRONMENTAL PROTECTION AGENCY GENE-TOX PROGRAM.

Legator MS, Bueding E, Batzinger R, Connor TH, Eisenstadt E, Farrow MG, Ficsor G, Hsie A, Seed J, Stafford RS
Dept. Preventive Medicine and Community Health, Div. Environmental Toxicology, Univ. Texas Medical Branch, Galveston, TX, 77550
Mutat Res; 98(3):3[illegible]9-3[illegible]4 1982

### 25. THE PHYSIOLOGICAL IMPORTANCE OF THE COLONIC MICROFLORA.

Gustafsson BE
Dept. Germfree Res., Karolinska Inst., Box 60 400, S-104 01 Stockholm, Sweden
Scand J Gastroenterol [Suppl]; 17(77):117-131 1982

### 26. AN ASSESSMENT OF THE ROLE OF MICRODOSIMETRY IN RADIOBIOLOGY.

Goodhead DT
Medical Res. Council Radiobiology Unit, Harwell, Didcot OX11 ORD, England
Radiat Res; 91(1):45-76 1982

## OTHER REVIEWS IN CARCINOGENESIS

### 27. PSYCHOSOCIAL ASPECTS OF CANCER.

Cohen J, Cullen JW, Martin LR
Sch. Social Welfare, Univ. California, Los Angeles, Los Angeles, CA
Psychosocial Aspects of Cancer. New York, Raven Press, 320 pp., 1982

☆U.S. GOVERNMENT PRINTING OFFICE: 1982-3[illegible]1-847/205

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